Disease course and healthcare burden of thymidine kinase 2 deficiency (TK2d) in Rady Children's Hospital patients

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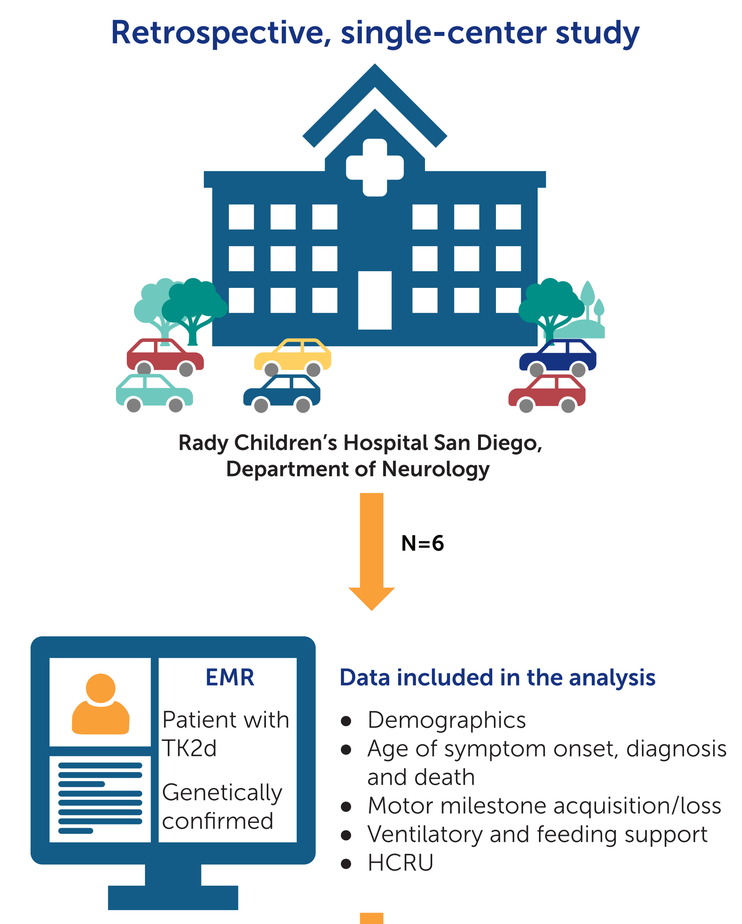
Introduction

- Thymidine kinase 2 deficiency (TK2d) is an ultra-rare, life-threatening, genetic mitochondrial disease caused by autosomal recessive pathogenic variants of the thymidine kinase 2 gene (*TK2*)[1,2]
  - The estimated prevalence of TK2d (first quartile [Q1], third quartile [Q3]) is 1.64 (0.5, 3.1) cases per million people and the number of patients with TK2d (Q1, Q3) in the USA is estimated at ~550 (170, 1040) when applying this prevalence[3]
  - TK2d is often mistaken for other neuromuscular and mitochondrial myopathies, and genetic testing is usually required to confirm diagnosis[1,2,4]
- While the clinical presentation of TK2d varies by age of symptom onset, most patients exhibit progressive muscle weakness that often leads to use of ventilatory and feeding support[1,2,4,5]

Objective

- The aim of this retrospective study was to describe the disease course and healthcare resource utilization (HCRU) in a cohort of patients with TK2d at Rady Children's Hospital San Diego (RCHSD) (**Figure 1**)

Figure 1. Study design



EMR, electronic medical record; HCRU, healthcare resource utilization; TK2d, thymidine kinase 2 deficiency.

Methods

- Data were extracted from electronic medical records (EMRs) of patients with TK2d seen at the Department of Neurology of RCHSD between November 1991 and December 2025
  - Data collection took place between April 2025 and December 2025
- The study was reviewed by an institutional review board and determined to meet the criteria for a waiver of informed consent in accordance with applicable US federal regulations (45 CFR 46.116(f), 2018 Common Rule; and 45 CFR 46.116(d), pre-2018 requirements)
- The following data were collected, deidentified and extracted
  - Patient demographics, comorbidities and disease history
  - Developmental motor milestones (gain or loss of ability to hold head upright unassisted, to roll unassisted, to sit upright unassisted, and to stand, walk, climb stairs, jump or run)
  - History of ventilatory and feeding support
  - Results of relevant laboratory tests (genetics/genomics testing, muscle biopsies and creatine kinase [CK] levels)
  - History of patient visits (physician specialty, hospitalization, emergency room visits and types of appointments) and medication
- The study analysis included all information from the earliest data available for each patient until patients were either lost to follow-up or the end of December 2025, whichever came first
  - The index date for this study was defined as the date of the earliest documentation or EMRs available for each included patient

Results

Patient demographics and disease characteristics

- In total, six patients with TK2d were seen at the Department of Neurology of RCHSD during the period studied
- Patient demographics and disease characteristics are shown in **Table 1**
- The mean (minimum, maximum [min, max]) age of symptom onset was 3.6 (1.9, 8.0) years (N=6), and first reported symptoms included: falling or difficulty walking (n=3), proximal muscle weakness (n=2) and loss of mobility (n=1); all patients had achieved normal motor milestones before symptom onset
- Before diagnosis, all six patients underwent CK testing and muscle biopsies
  - Muscle biopsy findings included: cytochrome c oxidase-negative fibers, fiber size variation, type I fiber predominance and dense connective tissue
- Patients (N=6) received a mean (min, max) of 3.7 (2.0, 6.0) alternative differential diagnoses before a TK2d diagnosis, including dystrophies and other neuromuscular and mitochondrial diseases
- TK2d was confirmed by genetic testing in five patients at a mean (min, max) age of 16.1 (7.7, 23.7) years
  - For patients with available molecular characterization data (n/N=5/6), all were homozygous (or apparently homozygous) for their confirmed *TK2* genotype and two harbored the c.173A>G (p.Asn58Ser) variant
  - Other *TK2* genetic variants included: c.323C>T (p.Thr108Met) and c.360_361del[GCinsAA] (pHis121Asn), both of which were identified in exon 5
- At data analysis, all six patients (100%) were wheelchair users
- In total, 4/6 patients (66.7%) were ventilator dependent; however, all six patients (100%) were using some form of ventilatory support
  - The mean (min, max) age when ventilatory support started was 11.9 (8.7, 14.4) years for all patients (N=6), and the mean (min, max) age when ventilator dependency started was 15.1 (12.2, 18.4) years for patients who were ventilator dependent (n=4)

Table 1. Patient demographics and disease characteristics

Characteristic	Patients with TK2d (N=6)
Sex, female, n (%)	3 (50.0)
Ethnicity, Hispanic/Latino, n (%)	6 (100)
Age of symptom onset, category, n (%)	
≤2 years	2 (33.3)
>2–12 years	4 (66.7)
>12 years	0 (0.0)
Age of symptom onset, mean (min, max), years	3.6 (1.9, 8.0)
Age of first visit at RCHSD, mean (min, max), years	4.1 (0.25, 7.7)
Age at data collection, mean (min, max), years	26.3 (12.4, 36.2)
Suspected diagnosis before TK2d confirmed, n (%)	
Congenital muscular dystrophy	4 (66.7)
Collagen 6-related dystrophy	3 (50.0)
Mitochondrial myopathy	3 (50.0)
Myofibrillar myopathies or other degenerative myopathies/dystrophies	2 (33.3)
Limb girdle dystrophy	2 (33.3)
Congenital myopathies due to suspected mutations in *FHL1*/*MEGF10*	1 (16.7)
COX-negative non5q SMA	1 (16.7)
Gamma dystroglycanopathy	1 (16.7)
Mitochondrial neuropathy	1 (16.7)
mtDNA depletion syndrome	1 (16.7)
Number of CK tests before TK2d diagnosis, mean (min, max), per patient	4.2 (1.0, 10.0)
Age at first CK test, mean (min, max), years	11.0 (4.0, 23.1)
Age at muscle biopsy, mean (min, max), years	8.3 (3.0, 18.7)
Diagnosis of TK2d, n (%)	
Confirmed by genetic testing	5 (83.3)
Confirmed indirectly (affected sibling)	1 (16.7)
Age at molecular diagnosis of TK2d,[a] mean (min, max), years	16.1 (7.7, 23.7)
Time from symptom onset to molecular diagnosis of TK2d,[a] mean (min, max), years	12.5 (5.5, 21.2)
Wheelchair user, n (%)	6 (100)
Age at initiation of wheelchair usage, mean (min, max), years	7.0 (4.0, 12.2)
Ventilator use, n (%)	
Ventilator dependent	4 (66.7)
Ventilatory support used	6 (100)
Age at initiation of ventilatory support, mean (min, max), years	11.9 (8.7, 14.4)

n indicates number of patients.
[a]n=5 because no direct molecular confirmation was available for one patient (diagnosis was confirmed indirectly via an affected sibling).
CK, creatine kinase; COX, cytochrome c oxidase; *FHL1*, four and a half LIM domains 1 gene; max, maximum; *MEGF10*, multiple epidermal growth factor-like domains 10 gene; min, minimum; mtDNA, mitochondrial DNA; RCHSD, Rady Children's Hospital San Diego; SMA, spinal muscular atrophy; TK2d, thymidine kinase 2 deficiency.

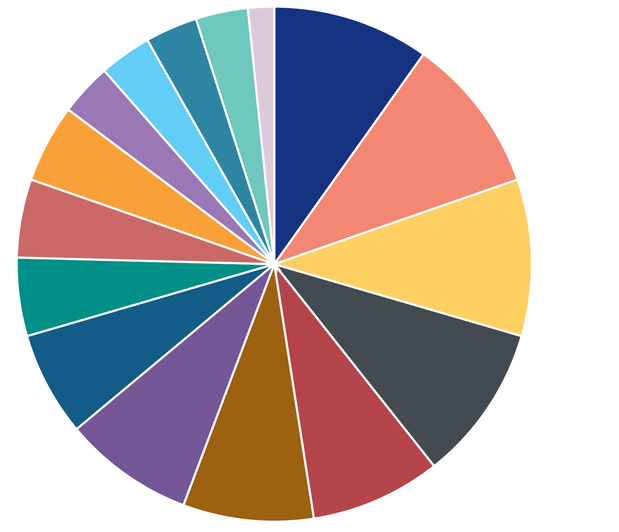
Healthcare resource utilization

- Without adjustments for follow-up time (N=6), the overall mean (min, max) number of hospital stays was 8.5 (0.0, 23.0) per patient, with each admission lasting 8.2 (0.0, 16.7) days
- All patients (N=6) had a mean (min, max) of 0.6 (0.0, 1.3) hospital stays per year from symptom onset to last follow-up visit and 0.5 (0.0, 0.8) hospital stays per follow-up year
- Patients with a definitive molecular diagnosis via genetic testing (5/6) had a mean (min, max) of 0.4 (0.0, 1.1) hospital stays per year from symptom onset to molecular diagnosis and 1.9 (0.0, 5.5) hospital stays per year from molecular diagnosis to last follow-up visit
- For all six patients, the mean (min, max) number of outpatient visits per follow-up year was 91.3 (8.1, 216.2)
- After receiving a TK2d diagnosis, all six patients consulted physicians from multiple specialties (**Figure 2**)

Patient follow-up

- At the point of data analysis, the total follow-up time for all six patients was 111.7 person-years
- Three patients (3/6; 50.0%) transitioned to adult care from pediatric care and their status is currently 'lost to follow-up'
  - The mean (min, max) follow-up time for these patients was 24.0 (21.1, 27.1) years
- For the remaining patients (3/6; 50.0%), active follow-up continues
  - As of December 2025, the mean (min, max) follow-up time for these patients at data analysis was 13.2 (6.3, 17.0) years

Figure 2. Specialist consultations after diagnosis of TK2d



n indicates number of patients.
[a]Other specialties seen by one patient included: cystic fibrosis, endocrinology, genetics, gynecology, pain medicine, psychiatry, scoliosis clinic.
TK2d, thymidine kinase 2 deficiency.

Conclusions

This study makes an important contribution to the limited knowledge of the clinical course of TK2d and associated HCRU patterns

The mean time interval of 12.5 years between symptom onset and a definitive molecular TK2d diagnosis via genetic testing underscores a significant unmet need for early diagnosis

The variety of specialties involved in patient care highlights the heterogeneity of TK2d and the complex needs of patients with this rare disease

The overall mean of 8.5 hospital stays per patient and mean length of stay of 8.2 days per admission emphasize the substantial HCRU burden associated with the management of patients with TK2d

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References: 1. Berardo A, *et al. J Neuromuscul Dis* 2022;9:225–35. 2. Garone C, *et al. J Med Genet* 2018;55:515–21. 3. Ma Y, *et al.* Poster EPH140. Presented at ISPOR 2023, November 12–15, 2023; Copenhagen, Denmark. 4. Wang J, *et al. TK2*-related mitochondrial DNA maintenance defect, myopathic form. In: Adam MP, *et al.* eds. *GeneReviews®* [Internet]. Seattle (WA): University of Washington, Seattle; 2018. 5. Martins Moreno CA, *et al. Sci Rep* 2025;15:9013.

Disclosures: Sarah Chang is an employee of and stockholder in UCB. **Yuanjun Ma** is an employee of UCB. **Edwin F Juárez**, **Laura E Tobin**, **Hung Nguyen** and **Erica Sanford Kobayashi** have nothing to declare.

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