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Case Report

Management of a urea cycle disorder in the setting of socioeconomic and language barriers☆

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ABSTRACT

Argininosuccinic aciduria (ASA) is a disorder that results from a deficiency in the urea cycle enzyme argininosuccinate lyase. Variable manifestations of this hereditary disorder are associated with hyperammonemia and can include lethargy, somnolence, and respiratory alkalosis in neonates, and vomiting, headaches, and neurocognitive deficiencies later in life. Management of ASA includes rapid measures to address hyperammonemia and long-term steps to maintain metabolic stability. Management paradigms should also consider social determinants of health, which are non-medical factors that influence health outcomes. Here, we describe the case of a male pediatric patient with ASA whose treatment has included considerations for his family's refugee status, language barriers, cultural adjustments, limited income, and transportation challenges.

1. Introduction

Urea cycle disorders (UCDs) are a group of inherited metabolic diseases that can result in life-threatening hyperammonemia. UCDs are caused by deficiencies in any 1 of 6 enzymes or 2 transporters of the urea cycle pathway and have an annual incidence of 1 in 35,000 in the United States [1,2]. The urea cycle enzyme argininosuccinate lyase (ASL; EC 4.3.2.10) is responsible for producing arginine and fumarate from argininosuccinic acid [3]. Deficiency in ASL causes argininosuccinic aciduria (ASA; OMIM #207900), the second most common type of UCD, which may present at any time of life with variable manifestations [3,4]. Neonates with severe hyperammonemia may present with lethargy, somnolence, vomiting, tachypnea, difficulty feeding, and respiratory alkalosis. Lack of prompt treatment leads to increasing lethargy, seizures, coma, and possibly death. Throughout the lifespan, hyperammonemia can be triggered by acute infection or stress, with symptoms such as vomiting, self-restriction of protein, headaches, behavioral abnormalities, and/or learning disabilities, in the possible absence of any known hyperammonemic crises [4–7].

Treatment of ASA is similar to that of other UCDs and includes rapid measures to address hyperammonemia during metabolic decompensation as well as long-term management to help prevent hyperammonemia and the neurologic complications that can result from even subthreshold chronically elevated ammonia [3,8,9]. The pillars of long-term management include dietary restriction of protein; supplementation with essential amino acids, vitamins, and arginine; and, if needed, oral nitrogen-scavenging therapy [3]. Evolving treatment options and increased understanding about the impact of UCDs have led to generally positive outcomes for patients who are regularly monitored by a multidisciplinary care team. However, given the risk of a fatal hyperammonemic crisis and long-term sequelae of elevated ammonia, persistent and mindful care is required.

Despite improvements in genetic metabolic disease diagnosis and management, health disparities persist and impact health outcomes

Abbreviations: ASA, argininosuccinic aciduria; ASL, argininosuccinate lyase; DME, durable medical equipment pharmacy; DSCC, Department of Specialized Care for Children; EAA, essential amino acid; GIR, glucose infusion rate; IV, intravenous; NICU, neonatal intensive care unit; NORD, National Organization for Rare Disorders; PICC, peripherally inserted central catheter; PICU, pediatric intensive care unit; PO, by mouth; QID, 4 times a day; SDOH, social determinants of health; UCD, urea cycle disorder.

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[10]. Optimized management of UCDs ideally considers social determinants of health (SDOH; ie, non-medical factors) related to the patient and the family unit, including financial constraints, limited language or health literacy, and cultural barriers [10–12]. Management success may be further complicated because of the rarity of UCDs. Patients and caregivers must overcome misconceptions and limited awareness about the condition among society and health care professionals [13]. For example, assistance programs like local food banks may place limits on medically necessary low-protein food items, and caregivers may be questioned as to why children are not being offered more protein, a necessary aspect of diet for many healthy individuals. Similarly, educators and evaluators may mistake early signs of hyperammonemia for attention-deficit/hyperactivity disorder, leading down a path of ineffective support services [6].

Here, we describe the case of a male pediatric patient with ASL deficiency who presented symptomatically at birth. The patient's management approach has required consideration of the family's journey as refugees, including language barriers, cultural adjustments, lack of close family support, limited income, and transportation challenges. By sharing our clinic's process in navigating various health inequities that this family has faced, we hope to bring greater attention to the importance of identifying and accommodating social determinants of health in rare metabolic disease management plans.

2. Case presentation

2.1. Patient presentation and diagnosis

Our patient is a 7-year-old child of refugee Zomi parents who was born at an academic hospital in a major city. The patient's father completed high school in Burma and speaks Burmese and English. He emigrated from Myanmar 3 years prior to his son's birth. The patient's mother completed middle school in Burma and speaks only Burmese. She arrived from Malaysia 1 year prior to the patient's birth. Both parents immigrated via different agencies that were initially helpful, but were no longer involved with the family by the time of the child's birth. The parents expressed difficulties assimilating to a new country, an unfamiliar health care system, challenges with health literacy and language barriers. The patient's mother experienced complications during pregnancy, including insulin-dependent gestational diabetes and latent tuberculosis. She was followed by infectious disease and maternal-fetal medicine specialists and was admitted to the hospital at 33w3d from a routine obstetrics appointment due to variable decelerations on fetal monitoring with maternal contractions. The patient was born at 34w1d and was vigorous at birth with Apgar scores of 9 and 9.

At 1 h of life, he developed tachypnea and persistent desaturations requiring high-flow oxygen. Septic workup results were unremarkable, but he received 2 days of empiric antibiotics. At 3 days of life, the patient was transferred to the NICU, where he developed poor feeding, lethargy, and apneic episodes that prompted repeat septic workup and initial metabolic workup. Metabolic workup results showed hyperammonemia (>1400 μmol/L; reference range < 150 μmol/L) and increased oxygen requirement. The patient became minimally responsive to stimuli and was intubated. The genetics team was consulted, and the decision was made to transfer him to the hospital's tertiary PICU due to acute hyperammonemic encephalopathy. Upon admission at 4 days of life, the patient's ammonia level was 1305 μmol/L (reference range < 150 μmol/L).

Before speaking with the parents, the critical care attending physician discussed options for attempting dialysis with the attending nephrologist and interventional radiologist on call. He then spoke with the parents at length through an interpreter about the risks and benefits of pursuing dialysis to treat hyperammonemia. Based on the neonate's prematurity and birth weight (2.2 kg), hemodialysis was considered challenging due to the large catheter size needed. Extracorporeal membrane oxygenation was also considered. The parents expressed their understanding that without dialysis, their son would likely have severe brain injury and possibly die. After carefully considering the risks and challenges of dialysis and the possible chronic sequelae of this illness, they decided to forgo dialysis and instead continue medical management. Members of the PICU team, including a pediatric surgeon, were also consulted, and all were encouraged by rapidly decreasing ammonia levels and improved neurologic examination with initial treatment, which included an IV nitrogen scavenger (sodium phenylacetate/sodium phenylbutyrate), IV arginine (1.45 g in 10% dextrose, 0.66 g/kg/day), and lipids (2 g/kg in 25% dextrose) to provide 14.9 mg/kg/min GIR.

The patient was diagnosed with ASA during a genetics consultation on day 4 of life. Preliminary amino acid analysis (Table 1) was consistent with the diagnosis, as was the relatively rapid decrease in ammonia levels with initial treatment. The diagnosis was confirmed by genetic testing revealing a homozygous missense variant in the ASL gene NM_000048.4(ASL):c.707G > A (p.Arg236Gln) classified as pathogenic/likely pathogenic.

2.2. Initial UCD management

Throughout admission, dietary management goals were managed by a metabolic dietitan and included protein intake of 1.2 to 2.2 g/kg (50% EAA and 50% intact protein) and 120 to 145 kcal/kg [14]. Nutritional management was initiated at 129 kcal/kg, 0.5 g/kg of protein (EAA only). Breast milk, which had been discontinued during the initial decompensation, was reintroduced at 15 days of life. The patient was also prescribed sodium phenylbutyrate at 450 mg/kg/day QID. He was discharged at 4 weeks of life with a gastrostomy tube for all feedings and medications. Dietary management included a daily formulation of Cyclinex®-1, Enfamil® infant formula, 4 oz. of breast milk, and arginine powder (1.6 g). This combination provided 123 kcal/kg, 2 g/kg of protein (55% EAA, 45% intact protein) and 467 mg/kg of arginine.

Table 1
Laboratory findings (μmol/L [reference range]).

	Age													
	3 days	2 mo	5 mo	8 mo	10 mo	15 mo	18 mo	21 mo	22 mo	3 years	4 years	5 years	6 years	7 years
Ammonia [11–35]*	>1400[a]	33[b]	47	43[c]	99[c]	60[c]	54	133[d]	153[d]	53	44	53[e]	33	260[d]
Glutamine [376–709]	262	394	481	–	713	661	509	–	–	424	501	–	299	–
Citrulline [10–40]	1160	79	454	–	218	230	245	–	–	331	220	–	273	–
Arginine [6–140]	549	78	105	–	45	57	36	–	–	41	38	–	46	–
Ornithine [48–211]	286	72	47	–	28	30	24	–	–	24	22	–	49	–

*Upper limit of normal <150.
[a.] Newborn decompensation. [b.] Gastrostomy tube issue. [c.] Excess protein from food intake. [d.] Viral upper respiratory infection requiring corticosteroids.
[e.] Feeding issue, 3-day hospitalization.
Laboratory assessments were performed at every clinic visit, but ammonia levels were measured only if clinical signs or symptoms were identified (precipitating cause for hyperammonemia summarized in footnotes). In addition to data here, a comprehensive metabolic profile was obtained at every visit. Vitamin D and B12 were monitored every 6 to 12 months. Phenylbutyrate metabolite analysis was monitored annually [15].

Table 2
Clinical care conferences held with caregivers and an in-person interpreter.

Patient DOL	Care team members	Key educational points to discuss with caregivers
8	• Critical care team • Geneticist/Genetics APP • Social worker • Registered dietitian	Diagnosis and management principles of ASA • Explanation that ASA is a genetic condition that causes the body to be unable to metabolize protein, leading to accumulation of ammonia in the blood • Description of HA symptoms • Treatment of ASA
18	• Critical care team • Geneticist/Genetics APP • Social worker • Registered dietitian • Speech therapist	Daily management of ASA • Insertion of a gastrostomy tube and ongoing education on ASA and diet management
21	• Genetic counselor	• Inheritance of ASA
35	• Geneticist/Genetics APP • Registered dietitian • In-patient team	• Review of diagnosis and treatment, information about when to seek medical attention, and an emergency letter in anticipation of discharge
The patient was discharged at 37 days of life.		

APP, advanced practice provider; ASA, argininosuccinic aciduria; DOL, day of life; HA, hyperammonemia.
Disease state education was provided throughout the inpatient stay. Topics were taught by scaffolding education through multiple conversations. New topics were introduced or reinforced at the indicated cadence. An in-person interpreter was present for all sessions.

At various points during admission, the family met with members of the multidisciplinary care team, who provided detailed education (Table 2) along with an emergency letter with management instructions if the patient presented for care at an outside center. Follow-up was scheduled for 2 weeks after discharge. Reportedly, the family was given the wrong gravity feeding bags and presented at the emergency department 2 days after discharge due to inability to provide overnight feedings. Proper equipment was provided, and no additional concerns arose at the time regarding the parents' ability to provide feedings.

2.3. Monitoring and outcomes

After discharge, our patient had good interim growth and was metabolically stable at most visits. He was seen monthly for the first 6 months of life, then every 3 months through age 2.5 years, and then every 4 to 6 months through present at age 7 years. He was also seen regularly by physical, speech, and occupational therapists due to his prematurity. During the first 2 years of life, elevated ammonia was identified several times as part of routine laboratory assessments (Table 1). Sodium phenylbutyrate and arginine dosing was adjusted accordingly. The first elevation after discharge was detected at 7 months of age, coinciding with the introduction of solid foods. The second elevation was detected at 10 months of age, shortly after the registered dietitian was informed that the mother requested to increase solids. We updated our dietary recommendations based on this request while still highlighting the importance of <1 g of protein per serving.

Despite reinforcing education on low-protein options through an in-person interpreter and providing picture-based medication plans (Supplemental Fig. 1 and Supplemental Fig. 2), excessive protein intake from higher protein fruits and vegetables was identified from diet recall. Collaboration between the registered dietitian and speech language pathologist was initiated to help reinforce education. Texture progression and safe swallowing were discussed during speech therapy, and protein restriction education was deferred to the genetics team. Further education came through the family's primary care physician, who helped reinforce the management plan and documented that understanding was evaluated using the teach-back method through a Burmese interpreter. Importantly, use of a variety of low-protein foods increased once the registered dietitian placed an order for appropriate food from a local service that provides medically necessary low-protein foods.

At 21 months of age, our patient was hospitalized for 23 days with fever, cough, and decrease in PO nutrition. Ammonia was minimally elevated on admission but peaked at 133 μmol/L (reference range 11–35), necessitating central access to provide a higher GIR. The patient developed a viral upper respiratory infection and was intubated for sedation while undergoing PICC placement. Due to fever and an episode of stridor at rest with respiratory distresses, he was transferred to the ICU. He was stabilized with antibiotics and after weaning oxygen support was discharged on 210 mg/kg of arginine, 450 mg/kg/day of sodium phenylbutyrate, and 1.2 g/kg of protein. A second viral upper respiratory infection occurred a month later, also leading to hyperammonemia. Due to respiratory distress, both illnesses required treatment with corticosteroids. Before administering treatment, the genetics specialist was consulted and metabolic control was monitored to offset the impact of steroid administration, if needed.

Our patient was 3 years old in 2020 when the coronavirus disease 2019 (COVID-19) pandemic changed certain protocols, such as greater use of telemedicine and outpatient laboratories for routine monitoring. The family shared that the father's employment status was compromised, and they were facing food insecurity. They met with a social worker and obtained food assistance from a local food pantry. Additionally, in January 2020, the primary registered dietitian on the patient's team changed, and the patient's father consistently responded to requests for diet recalls/records by stating “his foods are all lowprotein, or fruits and vegetables.” This response has continued through subsequent years, and the parents have shared that they don't count protein intake.

By the time the patient began prekindergarten, he had global developmental delay but showed improvements in his expressive speech delay and gross and fine motor function. Based on his laboratory assessments at age 5 years and 2 months, sodium phenylbutyrate was increased to 600 mg/kg/day, prompting the family to share that they had been administering less than the prescribed amount. Due to significant gastrointestinal distress (ie, nausea) and concern for increasing metabolic demand and decreasing metabolic stability on sodium phenylbutyrate, the patient was transitioned to glycerol phenylbutyrate (10 mL/m^2/day).

When the patient was around 5 years old, his family began sharing concerns about him being aware of his differences from his peers. His father shared that he was eating more of the “family foods” (ie, possibly not low protein), encouraged by his younger unaffected brother. A diet recall was not provided, although a dislike of eggs was shared. Principles of low-protein management were reinforced (Supplemental Fig. 2). Through a video interpreter, it was relayed that the patient found it

difficult to step away from playing to take his formula and felt shame in using his gastrostomy tube around others or when outside of his home. Challenges with the gastrostomy tube were also the cause of an emergency department visit and overnight admission. One week before the admission, the patient was seen by his primary care physician, whose office reached out to DME to order additional supplies. The office was told that DME had already repeated confirmed shipments of gastrostomy tube supplies, but the family had not received them, presumably because the packages had been stolen after delivery. Another incident occurred a few months later, resulting in a 3-day hospital stay. During admission, a feeding error occurred due to a miscommunication about taking formula by gastrostomy tube versus by mouth. A family friend was at the patient's hospital bedside because the parents were not able to be, which potentially contributed to the error not being identified sooner.

2.4. Ongoing monitoring and management

The patient is now 7 years old. He has normal left ventricular function, mildly increased left ventricular mass with no hypertrophy and no systemic hypertension. He has no chronic hepatitis and has preserved liver synthetic function and fibrosis, noted by increasing elastography measurements. He has no trichorrhexis nodosa. He is followed by multiple specialists, including a hepatologist, cardiologist, ophthalmologist, otolaryngologist, pediatric surgeon, and audiologist. He receives physical, occupational, and speech therapies through his school for his global developmental delay and expressive language disorder. Although these visits are covered by government programs and Medicaid, finding childcare for the family's 2 other unaffected children, travel, scheduling, and time away from work have been large burdens for the family. For metabolic management, the patient currently is treated with glycerol phenylbutyrate (10 mL/m^2/day), 269 mg/kg L- arginine, a protein-restricted diet supplemented with low-protein foods and a medical formula containing a mixture of EAA and intact protein provided as cow's milk. Due to the absence of diet records, 70% of the patient's intact protein is provided in a formula mixture that provides 30% of the patient's estimated daily energy needs. His diet goal is 4 g of protein daily in combination with formula that totals an estimated daily intake of 0.92 g/kg/day total (45% EAA, 55% intact protein). He is seen at our metabolic clinic every 3 to 4 months, with frequent diet and medication adjustments based on growth and laboratory assessments.

3. Materials and methods

Medical records and clinical parameters were reviewed by the treating clinical team. Informed consent was obtained from our patient's parents for publication of this case.

4. Discussion

Awareness is increasing among health care professionals regarding the importance of SDOH, but execution of strategies to identify and navigate health inequities, especially in patients with rare diseases, remains challenging [12,13,19,20]. Extracting key information on a patient's social situation is a sensitive process, and some health care providers may prefer to focus on medical treatment and lifestyle counseling [19]. The addition of SDOH related Z codes to the International Classification of Disease (ICD) coding system is an important step to better understand and document health disparities in communities; however, these codes are not yet widely adopted and are not in place in the Genetics Division of our institution. In this patient case, we have detailed how exploring the SDOH affecting our patient and his family was inextricable from providing effective care (Table 3) [19]. In our experience, these factors should be assessed before transitioning a patient from the acute care setting to long-term management. Establishing trusting relationships early on and incorporating social workers, when possible, builds the foundation to support patients and their families throughout their care.

Nutritional management is a pillar of treatment for ASA, but medical food and low-protein modified foods can pose additional financial burdens on families [21]. In addition to financial barriers, necessary

Table 3
Barriers to equitable care and suggested support services.

Barrier	Support	Considerations
Family's primary language is not English	• In-person interpreter for visits and telephone interpreter for calls • Pictorial and/or translated patient education materials	• Translation services increase the length of visits • Accuracy of translations may be subjective • Reading literacy may be lower than verbal fluency, even in the patient's native language • Teach-back methods can confirm understanding • Availability of translators for less common languages is limited
Assimilation into an unfamiliar health care system and various cultural approaches to health care	• Early establishment of trust; inquire about their migration journey and previous interactions with health care providers • Connection with a social worker who approaches patients and families with empathy and compassion	• Illness can be perceived and spoken about differently by other cultures [16,17]; consider using the Cultural Formation Interview as a basis for conversation [18]
Housing insecurity	• Rent assistance programs	• May be limited to a single use or short time period
Transportation challenges	• Medicaid-arranged transportation • Parking fee assistance	• Companies may not be consistently reliable • Available languages often limited to English and Spanish
Limited access to medical food and/or food insecurity	• State/local-run programs (eg, DSCC, Lil's Dietary Shop) • NORD	• Programs may have limited hours or complex pickup procedures
Lack of family or community support	• Peer-to-peer patient programs • Patient education guides (eg, NUCDF or UCD in Common) • ParentWISE/PeerWISE programs • Mental health services	• Local community events to connect patients who have a UCD may not already exist and/or may not be available in other languages
Financial insecurity	• Ronald McDonald House Charities® • NORD UCD assistance • Social security disability, Medicaid • Local charities (eg, Tiana Fund)	• Some families may be anxious about accessing public benefits due to their immigration status or previous interactions with government officials

DSCC, Division of Specialized Care for Children; NORD, National Organization for Rare Disorders; NUCDF, National Urea Cycle Disorders Foundation; UCD, urea cycle disorder.
Many support services exist to address potential barriers; however, navigating these services often requires additional considerations and in-depth understanding of patient needs.

knowledge and resourcefulness to navigate complex health care systems can be daunting, especially for those without local family support systems. Although the patient's caregivers did not express that obtaining low-protein foods was a barrier, the variety of these foods in the patient's diet increased once our team found routes for sourcing and subsidizing costs. In our case, this was accomplished through Lil's Dietary Shop, a local store in Chicago that serves to fill the gaps in the availability of medical foods. The store is listed as a vendor with Illinois' Department of Specialized Care for Children (DSCC). DSCC is a federally funded division dedicated to providing services to the state's children living with special health care needs. Through this program, families can apply for benefits that include financial assistance for the cost of medically necessary low-protein foods.

In addition to connecting families with available resources, health care teams can prioritize treatment regimens by considering a patient's largest obstacles. For example, in this case, we prioritized our attention on low-protein diet and medical food since medication was already mostly supported through insurance and other resources. Continued needs such as transportation, childcare for the rest of the family, and housing, which may not be typically discussed with the metabolic team or well covered by insurance, can also be assessed. In this case, the patient and his family live a short distance from our hospital and transportation was provided by his father, who owns a car. Parking assistance was provided. When his father's work schedule prevented the father from attending appointments, his mother learned to navigate the train and Medicaid non-emergency medical transportation to clinic visits.

Language barriers can cause a myriad of challenges, particularly when the patient or caregiver's native language is uncommon. When available, use of live interpreters is ideal, and interpreter needs should be considered when scheduling the length of appointments. Longer appointment times are needed because dialogue must be repeated in 2 languages and translated dialogue is delivered in blunted segments, which can disrupt the natural flow of conversation. Comprehension of conversations should be checked by asking the patient to teach back provided guidance, a practice that is beneficial regardless of language barriers but can contribute to appointment length. In our experience, the accuracy of translations often came into question, an issue that is exacerbated by the rarity and complexity of UCDs. Translators regularly paused to ask the clinician to repeat or explain terminology. There also was an inequality in the number of words used in a patient's reply compared to the number of words used by the translator. Moreover, even with highly accurate translations, there are nuances in language that may be misrepresented. For example, our patient's "shame" regarding his gastrostomy tube was conveyed through a translator, but upon reflection, we wondered if "shyness" may have been a more precise translation. Language barriers, in addition to health literacy, must be considered in patient education materials as well. In Supplemental Fig. 1 and Supplemental Fig. 2, we highlight how we adapted materials for this family; ideally, we would have provided fully translated materials, but that was not an option available to us. Further, obtaining medical supplies, regardless of financial burden, can be more difficult for patients/caregivers when there are language barriers. For example, during formula shortages in 2022, our patient's mother would place an order by phone to the state formulary, but staff at the Illinois Department of Public Health do not have access to interpreters, which made it difficult for the mother to understand backorders or product substitutions.

Taking steps to increase provider collaboration (eg, between metabolic team members, specialists, primary care physicians, and schools) to align on patient education and support services can also be beneficial for management goals. In Illinois, DSCC can provide support with care coordination plans and communication between providers, but steps can be taken without state run programs as well. For example, our patient's primary care physician helped ensure the correct medical food and medication regimen was being followed at each visit. If there were discrepancies, the primary care physician personally reached out to a member of our team for clarification. In addition, school nurses can be valuable resources and can ensure that management plans are being followed during school hours.

Independent of other SDOH, caring for a chronically ill child impacts a family's ability to maintain employment and financial stability due to the number of medical appointments and hospital stays. This is an area where proactive social work to educate families on available assistance programs can be valuable. In this patient's case, a referral was made to NORD UCD assistance once we learned that he was not attending all of his appointments (eg, rehabilitation therapy and the second day of neuropsychological testing). Because of the amount of work the patient's father was missing due to his son's hospitalization and medical follow-up appointments, the family fell behind in rent and faced threat of eviction. Social workers arranged one-time rent assistance offered through the Tiana Fund to help avoid eviction for the whole family. Social workers also provided counseling on ways to manage the family's medical and financial needs by empowering the patient's mother to attend appointments by herself and giving the patient's father the option to join clinic visits by phone when he could not be there in person with his son.

Lastly, although identifying SDOH is a key step in improving health outcomes, it is also necessary to be aware of implicit bias that can affect patient–provider interactions. Evidence has shown that a patient's socioeconomic characteristics impact physician behavior and medical decision-making [22,23]. As we reflect on this patient's case, we noticed that maintenance of diet records was not discussed. Although it is common for families to not track protein intake closely, in hindsight, it is not clear if greater discussion about how and why to keep diet records was curtailed due to perceived language or literacy barriers.

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Consent for publication

Informed consent was obtained from the patient's parents for this work.

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Author statement

We the undersigned declare that this manuscript is original, has not been published before and is not currently being considered for publication elsewhere.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We understand that the Corresponding Author is the sole contact for the Editorial process. He/she is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs.

CRediT authorship contribution statement

Erika Vucko: Writing – review & editing, Writing – original draft. **Joshua Baker:** Writing – review & editing. **Karen Becker:** Writing – review & editing. **Kirsten Havens:** Writing – review & editing. **Katherine Arduini:** Writing – review & editing, Writing – original draft. **Soo Shim:** Writing – review & editing.

Declaration of competing interest

EV, JB, KH, KA, and SS have participated in advisory boards and/or received honoraria from Amgen Inc. EV has received consulting fees/honoraria from Takeda, BioMarin, and Sanofi Genzyme. JB is principal investigator for a clinical trial sponsored by Ultragenyx. He has received consulting fees/honoraria from Biomarin, Takeda, and Ultragenyx. KB has no conflicts to disclose. KH has participated in advisory boards and/or received honoraria from BioMarin. KA has been involved in clinical trials sponsored by Ultragenyx and Aeglea Therapeutics and has received honoraria from Vitaflo and Acer Therapeutics. SS has received consulting fees/honoraria from BioMarin.

Data availability

No data was used for the research described in the article.

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