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Expanding the Clinical Spectrum of Arboleda-Tham Syndrome

Neuroimaging Findings and Hematologic Manifestations

Jee Min Kim,[1] Yoon Sunwoo,[1,2] Haeryung Kim,[2] Young Ho Kim,[2] Jong Ho Cha,[2] Seungbok Lee,[1,2] Jung Min Ko,[1,2] Byungchan Lim,[2] Soo Yeon Kim,[1,2] and Jong-Hee Chae[1,2]

Correspondence
Prof. Kim
iidue@naver.com

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Abstract

Background and Objectives

Arboleda-Tham syndrome (ARTHS) is a rare autosomal dominant neurodevelopmental disorder caused by pathogenic variants in the lysine acetyltransferase 6A (*KAT6A*) gene, characterized by global developmental delay, severe speech impairment, craniofacial dysmorphism, and congenital heart defects (CHDs).

Methods

We retrospectively reviewed data from 14 patients with molecularly confirmed *KAT6A* variants evaluated at the pediatric neurology center of Seoul National University Children's Hospital between 2018 and 2024. Clinical, genetic, neuroimaging, and laboratory data were systematically analyzed to evaluate the phenotypic spectrum associated with ARTHS.

Results

Fourteen patients were identified, 79% of whom were male, with ages ranging from 2 to 14 years at the time of their last visit. Thirteen patients (93%) harbored late-truncating variants. Global developmental delay was universal, with marked speech impairment; most patients remained minimally verbal beyond age 5. Craniofacial dysmorphisms were observed in 11 patients (79%) and CHDs in 6 of the 10 assessed (60%). Notably, 3 of 11 patients (27%) exhibited hematologic abnormalities, ranging from transient neonatal neutropenia to severe aplastic anemia requiring hematopoietic stem cell transplantation. Brain imaging revealed type 1 Chiari malformation and white matter hyperintensities in 2 of the 10 assessed (20%), suggesting a broader neuroanatomic involvement. Radioulnar synostosis was observed in 1 patient, suggesting a possible expansion of the skeletal phenotype in ARTHS.

Discussion

Our study broadens the recognized clinical features of ARTHS by reporting diverse neuroimaging findings, skeletal anomalies including radioulnar synostosis, and hematologic manifestations such as transient neonatal neutropenia and severe aplastic anemia. These findings reinforce the need for multidisciplinary surveillance in ARTHS and suggest potential avenues for further investigation into the role of *KAT6A* in hematopoiesis, neurodevelopment, and skeletal formation.

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Supplementary Material

Introduction

In 2015, Tham and Arboleda independently identified variants in *KAT6A* as the cause of a neurodevelopmental disorder now known as Arboleda-Tham syndrome (ARTHS).[1,2] This rare genetic condition is characterized by developmental delays, severe speech impairment, microcephaly, craniofacial dysmorphism, and congenital heart defects (CHDs). Most cases arise from *de novo* truncating variants in *KAT6A*.[2,3]

[1]Department of Genomic Medicine, Seoul National University Hospital, South Korea; and [2]Department of Pediatrics, Seoul National University Children's Hospital, South Korea.

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Glossary

ARTHS = Arboleda-Tham syndrome; **ASD** = atrial septal defect; **CHD** = congenital heart defect; **gnomAD** = Genome Aggregation Database; **HAT** = histone acetyltransferase; **MYST** = MOZ, Ybf2/Sas3, Sas2, TIP60; **PDA** = patent ductus arteriosus; **VSD** = ventricular septal defect; **WES** = whole-exome sequencing.

KAT6A is located on chromosome 8 and encodes a protein, lysine acetyltransferase 6A, which belongs to the MOZ, Ybf2/Sas3, Sas2, TIP60 (MYST) family of histone acetyltransferases (HATs).[1] This enzyme plays a crucial role in chromatin remodeling by acetylating lysine residues on histones, regulating gene expression through chromatin structure modification.[4-6] Pathogenic variants in *KAT6A* disrupt the structure and function of its encoded enzyme, impairing its physiologic cellular role in gene regulation and leading to widespread effects on growth and development due to its role in controlling other genes.

To date, approximately 100 patients with ARTHS have been reported, with large cohorts primarily from Western countries and only a few case reports from Asia, describing their clinical, developmental, and psychological features.[3,7-10] However, data on imaging findings, hematologic manifestations, and the longitudinal course of the disorder remain limited. This single-center study presents cases of 14 Korean patients with ARTHS diagnosed using whole-exome sequencing (WES), with new observations that expand the clinical spectrum of this disorder. Notably, we highlight hematologic abnormalities and brain and skeletal features that have not been commonly reported for ARTHS to date.

Methods

Study Design and Participant Recruitment

This retrospective cohort study included 14 patients diagnosed with pathogenic *KAT6A* variants, who visited the Pediatric Neurology Department at Seoul National University Children's Hospital between January 2018 and October 2024. Inclusion criteria required molecular confirmation of a *KAT6A* variant through genetic testing and the availability of comprehensive medical records. Patients with incomplete clinical or genetic data were excluded.

Genetic Analysis

KAT6A variants in this cohort were identified through WES using Illumina platforms. The sequenced reads were aligned to the human reference genome (hg38) and processed, adhering to the Genome Analysis Toolkit best practices. Variant annotation was performed using ANNOVAR, focusing on rare, protein-altering variants with a population allele frequency below 0.001% based on the Genome Aggregation Database (gnomAD). Previously reported variants were identified by querying the Human Gene Mutation Database and ClinVar. Variant interpretation followed the guidelines established by the American College of Medical Genetics and Genomics and the Association for Molecular Pathology (ACMG/AMP).[11] Parental testing confirmed the *de novo* status in available cases. Subsequent analyses, including genotype-phenotype correlation, were restricted to variants classified as pathogenic or likely pathogenic. A detailed description of the WES analysis pipeline can be found in our previous publication.[12]

Clinical Data Collection, Literature Review, and Statistical Analysis

Clinical and demographic data were collected from electronic medical records, including clinical features, developmental milestones, laboratory tests, and imaging findings. Patients were classified as minimally verbal if they used fewer than 30 single words or word approximations, well beyond the typical age at first word acquisition, which is approximately 12 months.[13] A literature review using the PubMed database was conducted to identify relevant studies on *KAT6A* and ARTHS. The search was limited to articles published in English and focused on studies of humans. Keywords such as "*KAT6A*," "Arboleda-Tham syndrome," and related terms were used to capture a comprehensive set of publications. Relevant articles were selected based on their relevance to the genetic, clinical, and phenotypic aspects of the syndrome. The reviewed literature was used to support the interpretation of identified variants and to provide context for the clinical features observed in this cohort. We focused on previously studied cohorts that included at least 4 patients with truncating *KAT6A* variants to enable more meaningful comparisons and deeper insights into the associated phenotypic spectrum. Previous studies have compared patients based on early-truncating vs late-truncating variants, and we adopted a similar approach. Late-truncating variants introduce stop codons in the last 2 exons (exons 16 or 17), whereas early-truncating variants result in premature termination between exons 1 and 15.[3,13]

International Business Machines Statistical Package for the Social Sciences for Windows, version 29.0, was used for statistical analysis. A χ^2 test or Fisher exact test was applied for categorical variables. We considered a two-sided $p < 0.05$ to be significant.

Standard Protocol Approvals, Registrations, and Patient Consents

Ethical approval was obtained from the Institutional Review Board of Seoul National University Hospital (IRB No. 1101-110-353), and documented written informed consent was obtained from the patients' parents.

Data Availability

Data not provided in the article because of space limitations may be shared anonymized at the request of any qualified investigator for purposes of replicating procedures and results.

Results

Demographic and Clinical Characteristics

In our cohort of 14 patients with pathogenic *KAT6A* variants, we observed a male predominance (11 boys, 3 girls). Their median age at their first clinic visit was 1 year 3 months (range 1 month–6 years). Two patients initially presented with congenital hypotonia and multiple anomalies within their first 2 months of life, whereas the remaining patients were referred primarily for assessment of developmental delay. Their ages at their most recent examination ranged from 2 to 14 years (Table 1).

Detailed clinical manifestations of all patients collected at the last visit are listed in eTable 1. Developmental milestones were significantly delayed in all patients. The median age at independent sitting was 1 year 3 months (range 7 months–3 years), whereas the median age at independent walking was 2 years 10 months (range 1 year 8 months–9 years). All patients exhibited speech delay, with 3 of 5 patients older than 10 years at the most recent examination remaining nonverbal. One patient exhibited severe speech impairment, remaining nonverbal until 11 years but being able to express two-word sentences at 14 years. Growth abnormalities were prevalent, with 5 of 13 patients (38%) born small for gestational age and 7 of 13 patients (54%) showing failure to thrive.

Craniofacial abnormalities were common, with microcephaly present in 8 of 14 patients (57%). Craniosynostosis was present in 1 patient (7%) and plagiocephaly in 2 (14%). Facial dysmorphism was observed in 11 of 14 patients (79%), with common features including sparse eyebrows, hypertelorism, low nasal bridge, broad nasal tip, low-set ears, and retrognathia. Gastrointestinal problems, including feeding intolerance, constipation, or recurrent vomiting, affected 8 of 14 patients (57%). Among 10 patients who underwent echocardiography, 6 (60%) had CHDs, including acyanotic left-to-right shunt lesions such as patent ductus arteriosus (PDA), atrial septal defect (ASD), and ventricular septal defect (VSD). Two patients who had clinically significant defects and required interventional procedures had late-truncating variants. Skeletal dysmorphisms, including tapering fingers, polydactyly, overriding toes, and radioulnar synostosis, were present in 7 of 14 patients (50%). Cryptorchidism was present in 9 of 11 male patients (82%).

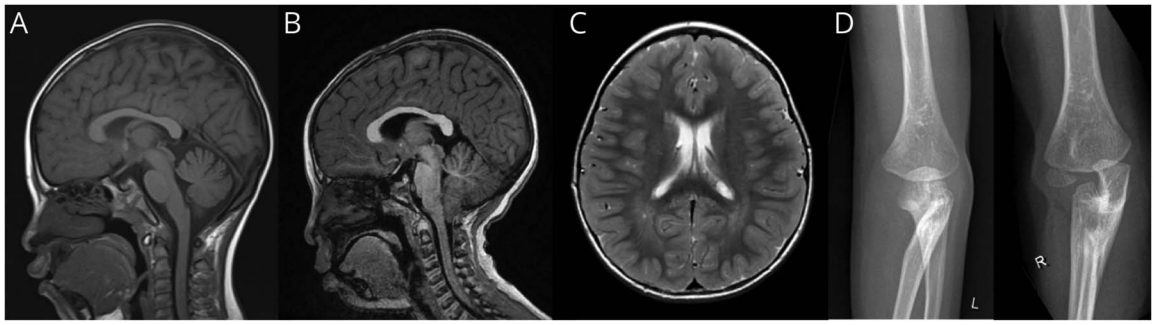
Notably, hematologic abnormalities occurred in 3 of 11 patients (27%) with available data. Two patients presented with transient neonatal neutropenia and thrombocytopenia, each of which resolved spontaneously by 6 months of age without complications such as sepsis, recurrent infections, or uncontrolled bleeding. One patient (patient 11) was diagnosed with severe aplastic anemia at 18 months of age, requiring repeated transfusions, and later underwent hematopoietic stem cell transplantation because of refractory thrombocytopenia at 40 months of age.

Among the 10 patients who underwent brain magnetic resonance imaging, normal findings were observed in 8 (80%) (Figure 1A), whereas type 1 Chiari malformation (Figure 1B)

Table 1 Clinical Features of Patients With Arboleda-Tham Syndrome

	Total (n = 14)
Age at first examination (median, min-max, y:m)	1:3 (0:1-6:11)
Age at last examination (median, min-max, y:m)	7:1 (2:2-14:11)
Sex, male (%)	11 (79)
Inheritance, *de novo* (%)	12/12 (100)
Growth (%)	
Small for gestational age	5/13 (38)
Failure to thrive	7/13 (54)
Motor development (%)	
Congenital hypotonia	7 (50)
Age at independent sitting (median, min-max, y:m)	1:3 (0:7-3:0)
Age at independent walking (median, min-max, y:m)	2:10 (1:8-9:0)
Speech development (%)	
Nonverbal	5 (36)
Minimally verbal	8 (57)
Verbal	1 (7)
Craniofacial manifestations (%)	
Microcephaly	8 (57)
Craniosynostosis	1 (7)
Plagiocephaly	2 (14)
Facial dysmorphism	11 (79)
Delayed tooth eruption	2 (14)
Brain structure abnormality	2/10 (20)
Ophthalmologic manifestations (%)	8 (57)
Gastrointestinal/feeding problem (%)	8 (57)
Congenital heart defects (%)	6/10 (60)
Hematologic abnormality (%)	3/11 (27)
Skeletal anomalies (%)	7 (50)
Cryptorchidism (%)	9/11 (82)
Behavior problems (%)	5 (36)
Sleep problems (%)	3 (21)

Figure 1 Brain MRI Scans and Elbow X-Rays of Patients With Arboleda-Tham Syndrome



(A) Normal sagittal brain MRI of patient 7 at 3 years of age. (B) Sagittal image of patient 11 at 3 years of age showing type 1 Chiari malformation without syrinx and (C) axial image showing T2 hyperintense signals of white matter in the peritrigonal area. (D) Anteroposterior elbow radiographs of patient 10 at 3 years of age, demonstrating radioulnar synostosis.

and white matter hyperintense signals in the peritrigonal area were identified in 2 patients (patients 10 and 11). T2 high signal intensity, resembling delayed myelination, was predominantly located in the posterior area (Figure 1C). Bilateral radioulnar synostosis was demonstrated on elbow anteroposterior radiographs of patient 10 (Figure 1D), obtained following radiography performed because of decreased range of motion in both elbows.

Genetic Findings

Genetic analysis identified truncating *KAT6A* variants in all 14 patients. Early truncation at exon 6 was identified in 1 patient, whereas 13 had late truncations. Six variants were previously reported as pathogenic in ClinVar, and 8 novel variants were classified as likely pathogenic by the ACMG guideline. None of the variants was found in the gnomAD population database. Among the 13 patients with late-truncating variants, 11 had truncations in the acidic glutamate/aspartate-rich domain and 2 in the serine/methionine-rich domain. Parental testing confirmed *de novo* origin in all 12 cases with available segregation data. One patient with an early-truncating variant had a truncation located within the MYST/HAT domain. No pathogenic variants were identified in other disease-causing genes among the patients.

Literature Review for Late-Truncating and Early-Truncating KAT6A Variants

A literature review was conducted to compare the phenotypes observed in our cohort with those reported in previously published studies. A large cohort including 76 patients from 3 cohorts was reported[3]: one referred by clinical geneticists, another from patient advocacy group registries, and a third identified through a literature review. Another study[14] described 5 patients with detailed phenotype descriptions. A further cohort[13] was notable for categorizing developmental delay into specific categories and for using standardized assessment tools to evaluate developmental status.

Our study and that of a previous report[14] showed a lower incidence of congenital hypotonia in patients with late-truncating variants than in another large cohort study[3] (Table 2). Speech delay remained a highly penetrant feature of ARTHS in all 4 studies, consistent with the characteristic developmental delays associated with *KAT6A* variants.[3,13,14] Ophthalmologic disorders, including strabismus, ptosis, and cortical visual impairment, were observed in a significant proportion of patients with late-truncating variants in the 4 studies. Gastrointestinal and feeding problems and CHDs were present in most patients with late-truncating variants. CHDs have been reported in 44–53% of patients with ARTHS, most commonly ASD (33%), PDA (17%), and VSD (7%).[3,5,13,15] Notably, one large cohort study[3] observed differing incidences of CHDs across variant types, with rates of 70%, 28%, and 0% among patients with late-truncating, early-truncating, and missense variants, respectively, and at least 45% of patients with CHDs required surgical or interventional treatments.

In our cohort, only 1 patient carried an early-truncating variant, making within-cohort comparisons limited. A literature review of early-truncating *KAT6A* variants revealed fewer cases presenting with congenital hypotonia, microcephaly, and CHDs, whereas speech delay remained highly penetrant (eTable 2).[3,13] Comparison between late-truncating and early-truncating variants using data from the literature review revealed a significantly higher prevalence of microcephaly (52% vs 5%, $p < 0.01$), CHDs (66% vs 22%, $p < 0.01$), and sleep problems (53% vs 23%, $p = 0.01$) in those with late-truncating variants (Figure 2 and eTable 3).

Discussion

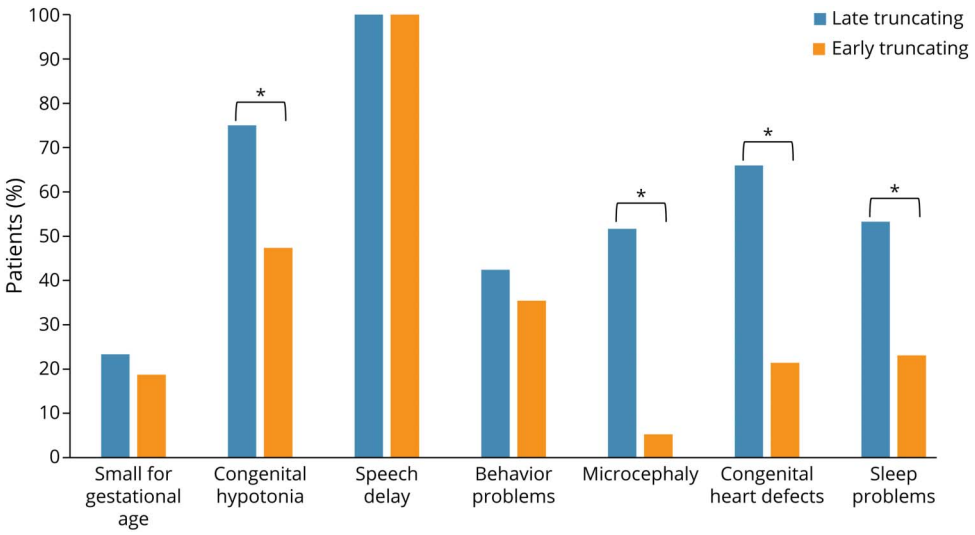
In this study, we comprehensively characterized 14 patients with pathogenic *KAT6A* variants, aiming to refine the clinical and molecular understanding of ARTHS. Our findings align with previously reported features while further delineating the phenotypic spectrum, particularly in hematologic and skeletal domains, and further clarifying genotype-phenotype correlations.

Table 2 Comparison of Late-Truncating Variants

	This study (n = 13)	Urreizti *et al*. (n = 4)	St. John *et al*. (n = 32)	Kennedy *et al*. (n = 48)
Sex, male (%)	11/13 (85)	2/4 (50)	16/32 (50)	23/48 (48)
Growth (%)				
Small for gestational age	4/12 (33)	2/4 (50)	n/a	8/44 (18)
Failure to thrive	6/11 (55)	4/4 (100)	n/a	n/a
Development (%)				
Congenital hypotonia	6/13 (46)	2/4 (50)	n/a	40/47 (85)
Speech delay (%)	13/13 (100) Minimally verbal 7/13 (54) Nonverbal 5/13 (38)	4/4 (100)	Minimally verbal 6/32 (19) Nonverbal 19/32 (59)	44/44 (100)
Behavior problems	5/13 (38)	2/3 (67)	13/32 (41)	8/18 (44)
Neurologic (%)				
Microcephaly	8/13 (62)	4/4 (100)	n/a	20/45 (44)
Facial dysmorphism	10/13 (77)	Broad nasal tip 4/4 (100) Thin upper lip 0/4 (0)	n/a	Broad nasal tip 35/40 (88) Thin upper lip 28/38 (74)
Ophthalmologic disorder (%)	8/13 (62)	Strabismus 4/4 (100) Visual defect 4/4 (100)	24/31 (72)	Strabismus 27/47 (57) Visual defect 26/38 (68) Ptosis 7/45 (16)
Gastrointestinal/feeding problem (%)	7/13 (54)	4/4 (100)	31/32 (97)	Feeding problem 40/46 (87) Reflux 27/38 (71) Constipation 18/28 (64)
Congenital heart defects (%)	6/9 (67)	4/4 (100)	18/32 (56)	32/46 (70)
Sleep problems (%)	3/13 (23)	1/4 (25)	22/32 (69)	15/28 (54)

This cohort demonstrated global developmental delay, with prominent speech delay and multisystem abnormalities. Most patients carried late-truncating variants, consistent with findings from other studies.[2,3,16] A key strength of this study is the comprehensive phenotypic assessment of our cohort, with most patients undergoing detailed clinical, imaging, and laboratory evaluations, which enabled more accurate genotype-phenotype correlations.

Figure 2 Joint Analysis for Comparison of Phenotypes Between Late-Truncating and Early-Truncating Variant Groups



Patients with late-truncating variants had significantly higher prevalence with microcephaly, congenital heart defects, sleep problems, and congenital hypotonia. For the comparison between late-truncating and early-truncating variants, data from 14, 4, 41, and 66 patients were combined from our study and those by Urreizti *et al*., St. John *et al*., and Kennedy *et al*., respectively.

Hematologic abnormalities are uncommon but have been reported in patients with ARTHS. In our study, patient 11 was diagnosed with severe aplastic anemia at 18 months of age and underwent hematopoietic stem cell transplantation at 40 months of age. These findings are consistent with those of a previous study, which suggested that *KAT6A* plays a crucial role in hematopoiesis by regulating the proliferation, differentiation, and quiescence of hematopoietic stem cells.[5] Transient neonatal neutropenia was observed in 2 patients in our study but resolved spontaneously. Similarly, another report[17] described a girl with intermittent neutropenia at 16 months of age, which resolved without intervention. However, severe hematologic complications may require medical intervention, including transfusions or hematopoietic stem cell transplantation. A further report[9] reported neonatal-onset pancytopenia in a 4-year-old girl, who was transfusion-dependent. Transplantation was recommended but declined by her parents. Based on these findings, we recommend routine complete blood count evaluations at the time of diagnosis and regular follow-up visits for patients with ARTHS to monitor potential hematologic complications.

Skeletal anomalies, including tapering fingers, polydactyly, and clubfoot, were observed in our cohort. Notably, radioulnar synostosis, identified in patient 10, has not been previously reported in individuals with ARTHS. Although craniosynostosis has been described as a rare craniofacial anomaly in a small number of patients,[3,14,18,19] upper limb skeletal fusions such as radioulnar synostosis have not been documented in the literature to date. Studies in animal and cellular models further support the role of *KAT6A* in skeletal development. A mouse model study demonstrated that mice with *KAT6A* deficiency exhibit vertebral abnormalities,[20] while another study[21] showed that *KAT6A* regulates osteogenesis through downstream pathways. Similarly, a further study[19] reported that *KAT6A* contributes to osteoblast differentiation. Collectively, these findings suggest that skeletal abnormalities may represent a component of the ARTHS phenotypic spectrum.

Previous studies on neuroimaging findings in ARTHS have reported diverse abnormalities, including a thin corpus callosum, pituitary abnormality, and absence of an olfactory bulb.[3,22,23] In our study, 2 patients with type 1 Chiari malformation also displayed signal changes in the peritrigonal white matter. A previous report[14] described a patient exhibiting type 1 Chiari malformation, polymicrogyria in the posterior right insula, and delayed myelination. Similarly, another study[24] described 2 patients with notable findings: one with type 1 Chiari malformation and the other presenting with cerebellar hypoplasia and reduced periventricular white matter. Two prior studies each reported a case of nonspecific hyperintense signal of white matter in T2/Fluid-Attenuated Inversion Recovery sequences.[14,22] The clinical importance of these white matter signal alterations remains uncertain and warrants further investigation. However, given the proposed mechanism of Chiari malformation as a mismatch between skull development and neural tissue volume,[25] dysfunction of *KAT6A* may affect skeletogenesis, contributing to these findings. These observations, along with patients showing plagiocephaly and microcephaly,[3,14,18,19] suggest that further research regarding its role in the skeletal development is needed.

Genotype-phenotype correlation in ARTHS has been discussed since 2015. Comparative analysis between our data and previous cohorts reveals that patients with late-truncating variants exhibit higher frequencies of congenital hypotonia, microcephaly, CHDs, and sleep problems. Speech delay was universally present in both early-truncating and late-truncating variant groups. A large cohort study[3] demonstrated that developmental delays and intellectual disability were more severe in the late-truncating group. Two prior studies reported that multiorgan involvement, such as reflux, constipation, and CHDs, was more prevalent in the late-truncating group.[3,14] A further study found that sleep disturbance, such as prolonged sleep onset and frequent awakenings, occurred only among patients with late-truncating variants,[26] consistent with our findings. A proposed explanation for severe phenotypes in patients with late-truncating variants is escape from nonsense-mediated mRNA decay, leading to the production of truncated *KAT6A* proteins.[3,5] These truncated proteins, lacking the acidic glutamate/aspartate–rich or serine/methionine domains, may result in dominant-negative or gain-of-function effects. The serine/methionine domain is known to mediate interactions with transcription factors that regulate transcription activation.[27] However, comparing phenotypes across different studies has inherent limitations, highlighting the need for long-term prospective studies in larger cohorts.

In our study, only 1 patient had an early-truncating variant at exon 6, making statistical comparisons between early-truncating and late-truncating variant groups infeasible. However, this patient achieved developmental milestones earlier than those with late-truncating variants, including walking and speaking meaningful words by 20 months of age. Among patients with late-truncating variants aged 5 years or older, most remained nonverbal. The youngest age at independent walking among patients with late-truncating variants was 2 years. These findings suggest that early-truncating variants may be associated with better gross motor and language development than late-truncating variants. A previous study[13] similarly reported that late-truncating variants were associated with more severe impairments in cognitive function, communication, daily living skills, and adaptive behaviors. However, another study[16] could not confirm these differences in cognition, behavior, emotional control, and social skills because of the small sample size.

Although genotype-phenotype correlations provided important clinical insights, our finding also suggest that predicting phenotypic outcomes based solely on genotype remains challenging in ARTHS. Patient 2 carries the same variant as 3

siblings reported in a previous study, each of whom presented with distinct features: persistent pulmonary hypertension of the neonate, recurrent pulmonary infections, and laryngomalacia. None of these features was observed in our patient. Patient 5 shares a variant previously reported in 2 cases. One case from a prior report[28] involved bilious vomiting on the first day of life, raising suspicion for intestinal obstruction, followed by an episode of subocclusion at 7 months of age. By contrast, our patient experienced only mild feeding difficulties that did not suggest pseudo-obstruction. In addition, a patient from another cohort study who had the same variant, presented with metopic craniosynostosis and severe constipation. These findings highlight that even among individuals with identical *KAT6A* variants, there can be considerable phenotypic variability, suggesting the influence of genetic modifiers or additional contributing factors on the expression of ARTHS.

This study expands the clinical spectrum of ARTHS through the characterization of 14 patients with pathogenic *KAT6A* variants. Consistent developmental delay—particularly in speech—was accompanied by multisystem involvement, including craniofacial, cardiac, gastrointestinal, hematologic, and skeletal abnormalities. Notably, we report radioulnar synostosis as a newly recognized skeletal feature and identify hematologic complications such as transient neonatal neutropenia and aplastic anemia. Brain imaging abnormalities, including type 1 Chiari malformation and white matter changes, were also observed.

These findings highlight the need for multidisciplinary and longitudinal surveillance and suggest potential updates to an existing guideline.[3,29] Specifically, they emphasize the importance of careful assessment of joint movement and consideration of surgical interventions in affected children.[3,29] In addition, regular hematologic evaluations for anemia, thrombocytopenia, and neutropenia should be incorporated into the clinical management framework for patients with ARTHS. Further studies are warranted to elucidate the role of KAT6A in neurodevelopment, hematopoiesis, and skeletal system formation, which may ultimately guide more targeted approaches to patient care.

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Author Contributions

J.M. Kim: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; analysis or interpretation of data. Y. Sunwoo: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. H. Kim: major role in the acquisition of data. Y.H. Kim: major role in the acquisition of data. J.H. Cha: major role in the acquisition of data. S. Lee: Study concept or design. J.M. Ko: major role in the acquisition of data; study concept or design. B. Lim: major role in the acquisition of data; study concept or design. S.Y. Kim: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data. J-H. Chae: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data.

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Disclosure

The authors report no relevant disclosures. Go to Neurology.org/NG for full disclosures.

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