CASE REPORT

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Rehabilitation in a Patient with Pantothenate Kinase-Associated Neurodegeneration: Observation of Gait Improvement in a Rare Disease with Three-Dimensional Gait Analysis

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ABSTRACT Pantothenate kinase-associated neurodegeneration is an inherited neurodegenerative disease consisting of brain iron accumulation in basal ganglia. Extrapyramidal symptoms are common. Gait and posture disorders are also observed, but characteristics of these disorders have not been identified in the literature. We shared our experiences about gait disorders in a patient with pantothenate kinase-associated neurodegeneration and the effectiveness of rehabilitation by using three-dimensional gait analysis. A better posture and walking stability are observed in this patient as a consequence of rehabilitation. Three-dimensional gait analysis is an objective tool to obtain quantitative gait data which helps to determine main requirements to improve the patient's gait and posture before planning rehabilitation.

Keywords: Pantothenate kinase-associated neurodegeneration; neurodegeneration with brain iron accumulation; gait analysis; rehabilitation

Pantothenate kinase-associated neurodegeneration (PKAN) or Hallervorden-Spatz disease, is a rare, neurological, autosomal recessive-inherited disorder and caused by a mutation in pantothenate kinase 2 (PANK2) gene which encodes pantothenate kinase enzyme and regulates biosynthesis of coenzyme-A.[1-5]

PKAN is mainly classified as classical and atypical subtypes.[2] Classical PKAN has a rapid and progressive process in the first decade. Dystonia is the major onset symptom accompanied by other extrapyramidal and pyramidal symptoms, cognitive, gait and postural disorders.[2,6,7] Atypical PKAN is a late-onset form presented with psychiatric, cognitive and speech disorders accompanied by less severe movement disorders in 2nd-3rd decades.[2,7] Eye-of-the-tiger sign is an important descriptive hallmark with a hyperintense area in the centre of globus pallidus, surrounded with hypointense rim (iron accumulation) in T2-weighted images of magnetic resonance imaging (MRI).[6] The diagnosis becomes clear after genetic confirmation.[2,6]

Gait may be affected by dystonia, rigidity, Parkinson-like symptoms, and postural disturbances; but characteristics of gait disorders have not been identified in the literature. A more objective tool to evaluate complex structure of gait is the combination of observational and three-dimensional gait analysis (3DGA) systems.[8,9] The main aim of this study was to share our experiences about gait disorders of a patient with PKAN and evaluate the effectiveness of rehabilitation on gait using 3DGA.

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A 29-year-old male patient's complaints began with some perseverations like increased frequency and duration of hand washing when he was 19. Over time, tremor, wobbling, stumbling, falling, dysphagia, dysarthria, hypophonia, and dystonia in jaw and left upper extremity appeared. He was a successful student, physically active person without gait and speech disorders previously. After cranial MRI findings and homozygous PANK2 gene c.401A>G (p.Glu 134 GLY) mutation in genetic tests, he was diagnosed with PKAN which was compatible with atypical subtype due to late-onset psychiatric symptoms with movement disorders. He was referred to our gait analysis laboratory with 4/5 motor deficiency in upper and lower extremity muscles in manual strength testing, bilateral clonus sign and limitation in right ankle dorsiflexion when knee was extended (5°) due to gastrocnemius muscle rigidity. 3DGA was performed using Vicon Bonita System (Oxford Metrics Ltd., Oxford, UK). Anthropometric measures (height, weight, leg length) were obtained. Thirty five retroreflective markers were placed on specific anatomical landmarks according to the Vicon's Plug-in-Gait model. The patient walked barefoot with his usual gait pattern on a 9-meters walkway. Data was processed on Vicon Nexus 1.8.4 program, spatio-temporal parameters and kinematics graphs were obtained using Polygon 4.0.1 software. Kinematic variables were described with respect to phases of gait cycle. Patient's data were compared with control data of our gait analysis laboratory.[10] Accordingly, strengthening, stretching, range of motion (ROM), balance, proprioception, endurance exercises, and gait training were planned. After 33-session rehabilitation, improvements were observed in muscles' strength (5/5), right ankle dorsiflexion (15°), and 3DGA.

Left leg stance phase percentage decreased and approached normal values, right leg stance phase percentage remained the same, double stance phase percentage of both legs decreased; decreased step and stride length increased after rehabilitation (Table 1).

Bradykinesia, decreased associated arm movements, hyperextended and left-bending trunk, inferiorly positioned left shoulder, increased lumbar lordosis were notable findings before rehabilitation in observational gait analysis.

In kinematic analysis; increased backward trunk lean (TL) in sagittal plane and ipsilateral TL toward left side in coronal plane during all gait cycles, decreased maximum hip extension in sagittal plane and excessive backward pelvic rotation on right side in transverse plane during terminal stance (TSt), excessive left hip abduction in coronal plane during stance, left knee hyperextension during midstance (MSt) and TSt, premature heel rise bilaterally during MSt, and decreased knee extension bilaterally at terminal swing (TSw) were observed (Figure 1, Figure 2, Figure 3).

After rehabilitation, we observed improvement in his trunk posture which was less hyperextended and left-shifted. His relatives emphasized their satisfaction with this better posture. Right hip extension during TSt increased, pelvic rotation and severity of knee hyperextension during stance decreased, exces-

TABLE 1: Temporal and spatial parameters.

	Before rehabilitation	After rehabilitation	Control data[10]
Walking speed (m/s)			1.00
Left	0.61	0.61	
Right	0.55	0.61	
Cadence (steps/min)			101
Left	76.9	68.5	
Right	78.1	72.9	
Step width (m)			0.15
Left	0.16	0.15	
Right	0.17	0.19	
Step length (m)			0.59
Left	0.44	0.57	
Right	0.42	0.50	
Stance phase (% of gait cycle)			60.8
Left	68.5	61.2	
Right	63.4	63.4	
Double stance phase (% of gait cycle)			19.2
Left	33.4	26.9	
Right	31.4	19.4	

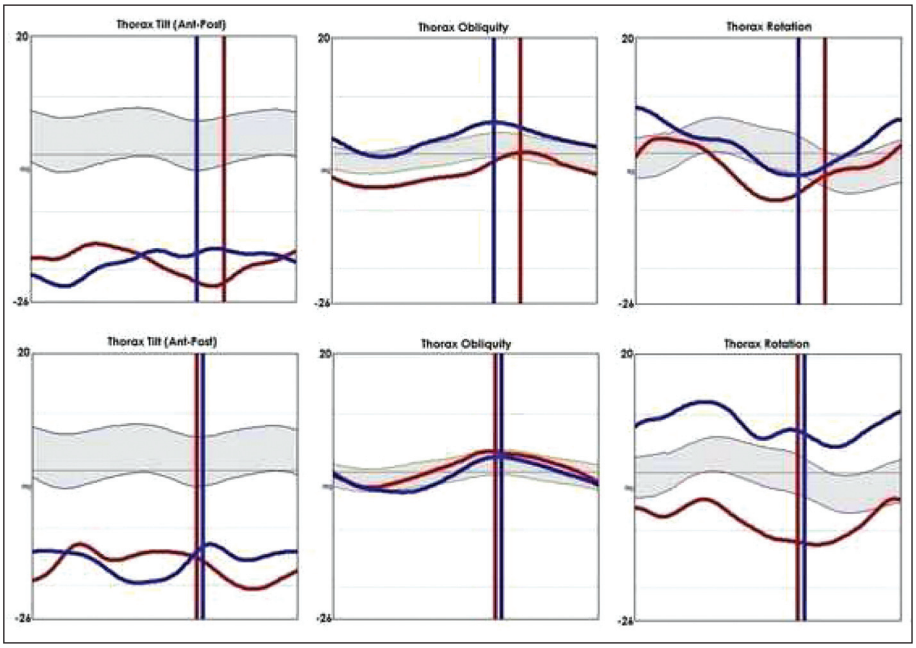

FIGURE 1: Kinematics of trunk: The gray area represents the normal kinematics. Red curve represents the kinematics of the left side of the trunk, blue curve represents the kinematics of the right side of the trunk. Graphs in the upper line show the kinematics before treatment, while lower line shows the kinematics after treatment.

sive left hip abduction during stance decreased and reached range of reference graph. Premature heel rise disappeared, bilateral knee extension during TSw, especially on left side, improved, and a better right ankle dorsiflexion during swing was observed.

Written informed consent was received from his father due to the patient's poor handwriting ability.

DISCUSSION

There is no accurate treatment that provides a cure or inhibits progression of PKAN. Therefore, treatment is generally based on clinical symptoms.[6,11] As well as medical and surgical treatments, it is valuable to protect or improve muscle strength and joint ROM which contributes to energy conservation and improvement in gait quality. Abnormal tone of muscles precipitate gait problems and limitations in joints that may result in contractures, spinal deformities, and hip dislocations. Reduced mobility due to musculoskeletal problems causes osteopenia and fractures. Thus, rehabilitation is important to protect patients from complications, keep them ambulatory as long as possible and provide participation in daily life. Rehabilitation programs include stretching, strengthening, and ROM exercises that should be supported by weight-bearing exercises to protect bone mass.[11] In the literature, there is no other study that shows the effectiveness of rehabilitation in neurodegenerative diseases with brain iron accumulation with 3DGA.

Normally, maximum hip extension in TSt and ankle dorsiflexion in MSt & TSt are needed to maintain center of gravity (COG) over foot for gait stability. Backward TL displaces COG behind hip joint to compensate hip extensor muscle weakness. Ipsilateral TL moves body weight toward hip joint center to compensate ipsilateral weak hip abductors. Decreased knee extension at TSw was related to ground reaction force (GRF) that passed behind knees due to backward TL or hamstring overactivity during TSw to compensate for primary hip extensor muscles' weakness. Inadequate knee extension during TSw shortens step length. After rehabilitation, with better stability and primary hip extensor and abductor muscle strength, above-mentioned findings improved. Excessive left hip abduction during stance is used for widening base support and increasing stance stability that decreased through improvement in ipsilateral TL and stability. Changes in spatio-temporal parameters

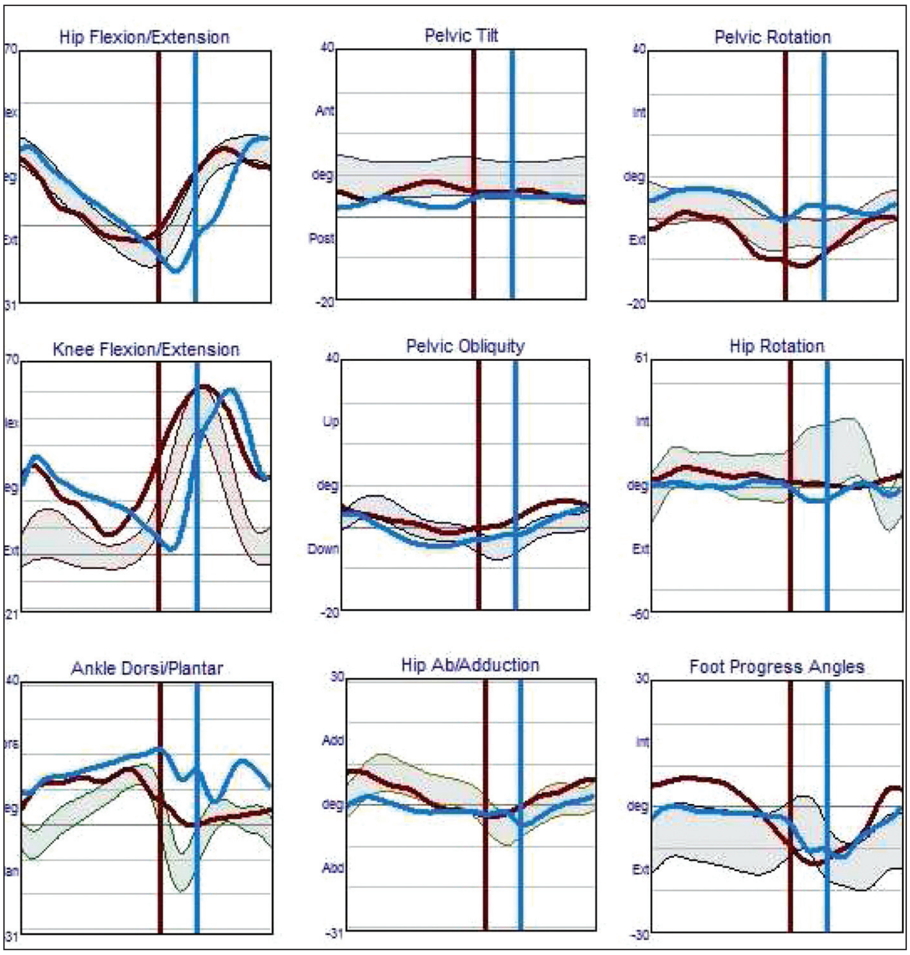

FIGURE 2: Kinematics of pelvis and right lower extremity: Kinematic variables of pelvis and right lower extremity in sagittal, coronal, and transverse planes are described with respect to the phases of gait cycle. The gray area represents the normal kinematics. Red curve represents kinematics of the right lower extremity before treatment, blue curve represents kinematics of the right lower extremity after treatment. Flexion (dorsiflexion) and adduction of the joints are positive values whereas extension (plantarflexion) and abduction values are negative.

also support increased stability. Left knee hyperextension during MSt and TSt causes body weight vector to pass anterior to knee joint that provides relative knee stability and reduces demand on weak quadriceps, but increases strain on the structures behind the knee.[12] Knee hyperextension disappeared with improvement on global muscle strength.

A detailed gait analysis of such a patient before and after rehabilitation is the most important feature of this report. 3DGA enables us to evaluate human locomotion comprehensively that cannot be evaluated with naked eye, determine rehabilitation strategies, and observe the effectiveness of treatments.[13] Before rehabilitation, the most remarkable disturbance was the trunk posture which was evaluated as a consequence of truncal dystonia. Through a better posture by decreasing backward TL, we observed an improvement in placement of GRF crossing lower extremity joints which ensured to achieve better stability. In this case, improving posture and stability are essential gains to prevent falls, fractures, and long-term problems.

Consequently, we should be aware of dynamic changes to prevent complications and improve quality of life. 3DGA should be considered in evaluation and follow-up of patients with neurodegenerative diseases. These patients should be encouraged for rehabilitation, according to their requirements, to decrease results of neurologic damage due to the nature of the disease.

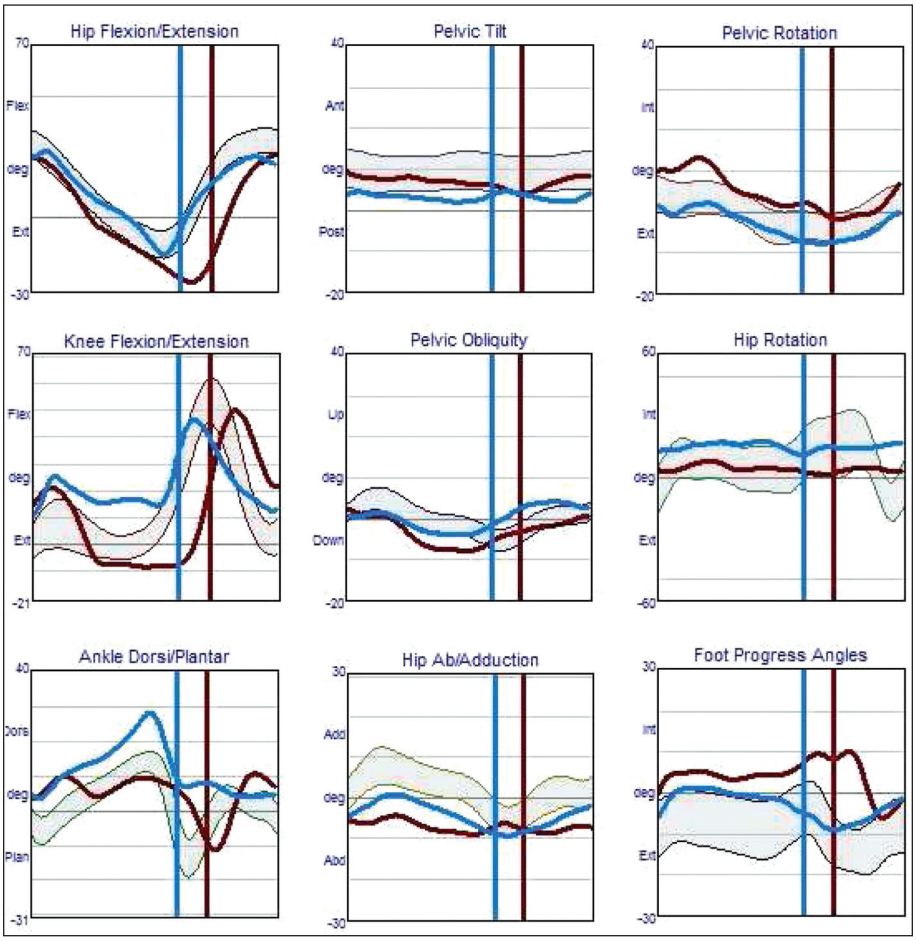

FIGURE 3: Kinematics of pelvis and left lower extremity: The gray area represents the normal kinematics. Red curve represents kinematics of the left lower extremity before treatment, blue curve represents the kinematics of the left lower extremity after treatment. Flexion (dorsiflexion) and adduction of the joints are positive values whereas extension (plantarflexion) and abduction values are negative.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

***Idea/Concept:** Aylin Sarı, Çiğdem Arifoğlu Karaman; **Design:** Çiğdem Arifoğlu Karaman, Sebahat Aydil, Aylin Sarı; **Control/Supervision:** Çiğdem Arifoğlu Karaman; **Data Collection and/or Processing:** Aylin Sarı, Çiğdem Arifoğlu Karaman, Sebahat Aydil; **Analysis and/or Interpretation:** Çiğdem Arifoğlu Karaman, Sebahat Aydil; **Literature Review:** Çiğdem Arifoğlu Karaman; **Writing the Article:** Çiğdem Arifoğlu Karaman, Sebahat Aydil; **Critical Review:** Çiğdem Arifoğlu Karaman, Sebahat Aydil.*

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