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# Delayed Onset of 16p11.2 Duplication Syndrome with Gait Disturbance: A Case Report

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## INTRODUCTION

**16p11.2 duplication syndrome** is a rare copy-number variant associated with diverse neurodevelopmental and neuropsychiatric features. The typical clinical manifestations of the syndrome include developmental delay, language impairment, behavioral abnormalities, hypotonia, tremors, or occasional seizures in early childhood. However, phenotypic expression of the syndrome is highly variable and rarely presents with delayed onset. In this report, we describe a patient with 16p11.2 duplication syndrome whose **clinical symptoms became apparent in adolescence.**

## CASE DESCRIPTION

### 12-year-old female

### Chief complaints

- **gait disturbance**

  : sudden onset of right lower extremity weakness upon waking one month earlier

### Past history

- family history (-)
- perinatal history (-)
- **developmental delay (-)**

### Physical examination

- manual muscle test

: **motor weakness on both lower extremities (MRC grade 3)**

- range of motion limitation (-)
- spasticity (-)
- pathologic reflex (-)
- **abnormal gait pattern during swing phase**
  - anterior pelvic tilt
  - slight knee flexion
  - ankle in equinovarus position
- Korean version of Berg balance scale: 49/56
- Korean version of modified Barthel index: 79/100

### Clinical timeline

**2025.01** Admission in orthopedic and neurology department
⇨ Sudden onset of right lower extremity weakness upon waking and gait disturbance

**2025.02** Brain & whole spine MRI
**: No significant abnormal findings**

**2025.02** Referred to
Physical and Rehabilitation medicine department

**2025.02** Electrodiagnostic study
**: No definite evidence of abnormalities**

**2025.02** Electroencephalography (EEG)
**: Normal awake, drowsy, and sleep EEG**

**2025.03** Gait pattern evolved into a waddling gait

**2025.04** **Somatic symptom disorder** was suspected as no structural abnormalities correlating with the patient's symptoms were found

**2025.09** Whole genome sequencing
: **Pathologic duplication on 16p11.2**
(arr[GRCh37]16p11.2 (29,615,949_30,177,224)x3)
⇨ Diagnosis) **16p11.2 duplication syndrome**

### Electrodiagnostic study

**Nerve conduction study**

| Nerve | Stimulation | Right Latency (ms) | Right Amplitude (Motor in mV Sensory in μV) | Right CV (m/s) | Right F-wave (msec) | Left Latency (ms) | Left Amplitude (Motor in mV Sensory in μV) | Left CV (m/s) | Left F-wave (msec) |
|---|---|---|---|---|---|---|---|---|---|
| **Motor** | | | | | | | | | |
| Median (APB) | Wrist | 3.0 | 16.3 | – | 22.3 | 2.7 | 14.7 | – | 22.1 |
| | Elbow | 6.7 | 15.6 | 57.6 | – | 6.1 | 14.4 | 59.1 | – |
| Ulnar (ADQ) | Wrist | 2.5 | 12.3 | – | 21.7 | 2.8 | 19.3 | – | 22.6 |
| | Elbow | 5.4 | 12.1 | 59.3 | – | 5.8 | 19.0 | 59.6 | – |
| Peroneal (EDB) | Ankle | 3.5 | 11.4 | – | 40.5 | 4.2 | 10.3 | – | 41.0 |
| | Below the fibular head | 9.3 | 10.2 | 51.4 | - | 9.8 | 9.4 | 49.8 | – |
| Tibial (AH) | Ankle | 3.0 | 35.5 | – | 40.3 | 3.3 | 33.2 | – | 40.9 |
| | Below the fibular head | 9.8 | 30.6 | 46.9 | – | 9.2 | 32.1 | 48.0 | – |
| **Sensory** | | | | | | | | | |
| Median | Wrist | 2.8 | 50.4 | | | 3.2 | 68.7 | | |
| Median | Midpalm | 1.7 | 52.7 | | | 1.7 | 64.0 | | |
| Ulnar | Wrist | 2.8 | 42.8 | | | 3.3 | 45.3 | | |
| Superficial Peroneal | Lateral leg | 3.8 | 14.2 | | | 3.8 | 15.4 | | |
| Sural | Calf | 3.4 | 16.6 | | | 3.3 | 17.9 | | |

**Needle EMG**

| Muscle | IA | ASA | MUAP | Recruitment pattern |
|---|---|---|---|---|
| **Right** | | | | |
| Tibialis anterior | Normal | Normal | Normal | Normal |
| Peroneus longus | Normal | Normal | Normal | Normal |
| **Left** | | | | |
| Tibialis anterior | Normal | Normal | Normal | Normal |

**SSEP**

| | Recording | Right Latency (ms) | Left Latency (ms) |
|---|---|---|---|
| Median nerve | Erb's point | 8.1 | 7.8 |
| | Cervical | 11.0 | 10.6 |
| | Cortex(N17) | 16.2 | 16.6 |
| | Cortex (P21) | 22.7 | 22.7 |
| Posterior tibial nerve | Popliteal fossa | 6.6 | 7.1 |
| | Thoracic | 18.1 | 18.5 |
| | Cortex (P37) | 35.5 | 35.2 |
| | Cortex (N45) | 44.0 | 44.9 |

**MEP**

| | Stimulation | Right Latency (ms) | Left Latency (ms) |
|---|---|---|---|
| APB recording | Cervical | 12.3 | 12.6 |
| | Cortical | 21.2 | 21.6 |
| AH recording | Lumbar | 19.5 | 19.5 |
| | Cortical | 34.8 | 34.5 |

Abbreviation; CV, conduction velocity; APB, abductor pollicis brevis; ADQ, Adductor digit minimi; EDB, extensor digitorum brevis; AH, Abductor hallucis; IA, insertional activity; EMG, electromyography; ASA, abnormal spontaneous activity; MUAP, motor unit action potential; SSEP, somatosensory evoked potential; MEP, motor evoked potential00

### Whole genome sequencing

**CHROMOSOME 16p11.2 DUPLICATION SYNDROME (OMIM: 614671)**

| Gene | Variant | Classification |
|---|---|---|
| SPN, QPRT<br>+ 25 more genes | **Genomic Position:** NC_000016.10:g.(?_29613103)_(30187223_?)dup(GRCh38)<br>**Cytogenetic band:** 16p11.2 (minimum size: 574.1kb)<br>**Type:** Duplication<br>**Zygosity:** Heterozygous<br>**Inheritance:** Unknown | Pathogenic |

## CONCLUSION

In this report, we describe a case of 16p11.2 duplication syndrome that was initially **misdiagnosed as somatic symptom disorder.** It was difficult to suspect a genetic condition because the symptoms emerged during early adolescence rather than childhood. This case highlights that **16p11.2 duplication syndrome can present somatic manifestations in a delayed manner.** Also, it suggests that **genetic testing should be considered in patients with unexplained symptoms.** Further research is needed about **diverse phenotypic spectrum of 16p11.2 duplication syndrome.**

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