PS-12

Cerebrotendinous xanthomathosis presenting with progressive gait disturbance and tendon xanthomas: A Case Report

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Introduction

- **Cerebrotendinous xanthomatosis (CTX)** is a rare autosomal recessive lipid storage disease.
- Patients with CTX are characterized by **childhood-onset cataracts** and **tendon xanthomas**, and **young adult-onset progressive neurological dysfunction.**
- Since **medication can delay its progression**, CTX should be diagnosed early.
- Here, we describe a case presenting with **progressive gait disturbance and tendon xanthoma** ultimately **diagnosed with CTX.**

Case Description

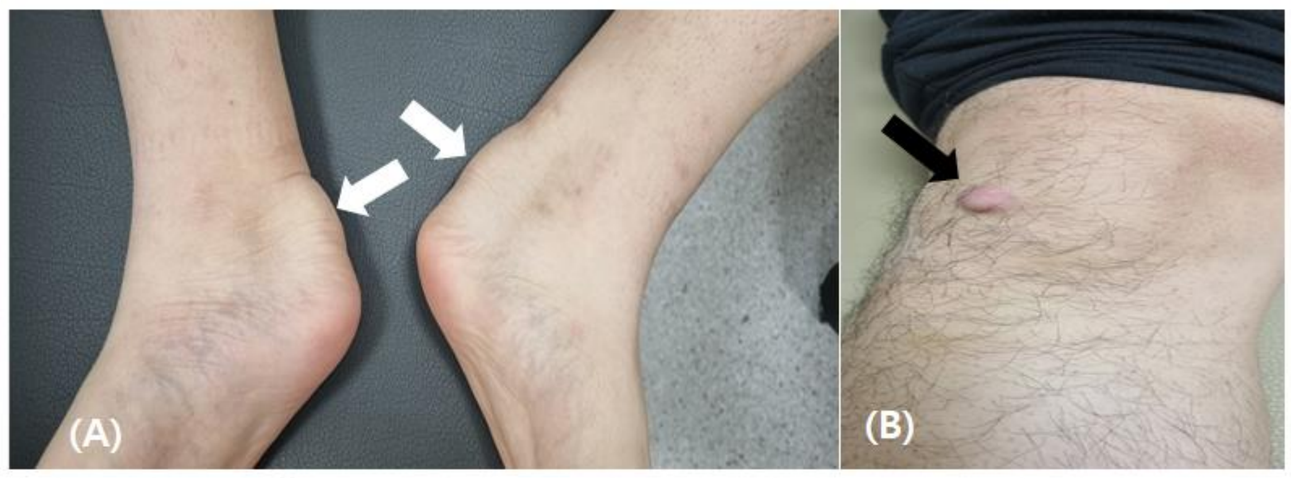
- A 33-year-old man visited the neuromuscular medicine clinic with a chief complaint of **progressive gait disturbance**, which developed 7 years ago. He had visited our clinic 6 years ago with same symptoms.
- There was no family history of gait disturbance. At that time, there was **no definite weakness**, but only **hypertonia in the lower limbs** (Table 1).
- Laboratory exams and lumbar spine magnetic resonance imaging (MRI) revealed no significant abnormalities explaining the symptoms.
- Also, no pathologic variant was found in SPAST gene analysis, so new generation sequencing (NGS) panel for hereditary spastic paraplegia (HSP) was performed. However, he didn't show up at the subsequent visit and the result could not be checked.
- When he returned to our clinic, **spastic gait had progressed**, and independent gait was difficult even with both canes. There was progression of weakness and spasticity in the lower limbs, along with **hyperreflexia in all four extremities** (Table 1).
- Electrophysiologic studies did not show findings suggesting peripheral neuropathy and brain MRI also showed no cortical or cerebellar atrophy.
- Additionally, **marked swelling of both Achilles tendons** and **small mass-like lesion in right knee** was observed, suggesting **xanthoma** (Figure 1).
- **Ankle MRI** showed findings consistent with **Achilles tendon xanthoma**, accompanied by thickening of the Achilles tendon (Figure 2).
- The previously conducted, NGS panel for HSP revealed the presence of a likely pathogenic variant and a variant of uncertain significance as heterogeneous variants in **CYP27A1 gene**. Genetic testing of his parents was recommended to determine if the variants are in trans.
- Due to the inability of enzyme assays for sterol 27-hydroxylase, sterol testing was conducted alternatively, but **the level of cholestanol (0.93mg/dL;<1.68) was normal.**
- Although the confirmative diagnosis of CTX was challenging based on the genetic and sterol testing, **considering the clinical manifestations** strongly suggestive of CTX, **mixtures of chenodeoxycholic acid and ursodeoxycholic acid** were prescribed.

Table 1. The result of neurologic exam

		1st visit (2017.06)	2nd visit (2023.11)
Motor strength (MRC grade)	Hip flexor	5- / 5-	1 / 2
	Knee extensor	5 / 5	2 / 2
	Ankle dorsiflexor	5 / 5	2 / 2
Sensory	Touch, pinprick	Intact	Intact
	Vibration	Intact	Intact
Spasticity (MAS)	Knee extensor	2 / 2	3 / 3
	Hip adductor	2.5 / 2.5	3 / 3
Deep tendon reflex	Biceps jerk	2 / 2	3 / 3
	Triceps jerk	2 / 3	4 / 4
	Knee jerk	4 / 4	4 / 4
	Ankle jerk	4 / 4	3 / 3
Pathologic reflex	Babinski reflex	+ / +	+ / +
	Ankle clonus	+ / +	+ / +
	Hoffman's reflex	+ / +	+ / +
Coordination	Rhomberg sign	Negative	Uncheckable
	Tandem gait	Instability (++++)	Uncheckable
	RAM	Intact / Intact	Intact / Intact
Autonomic dysfunction		No	No

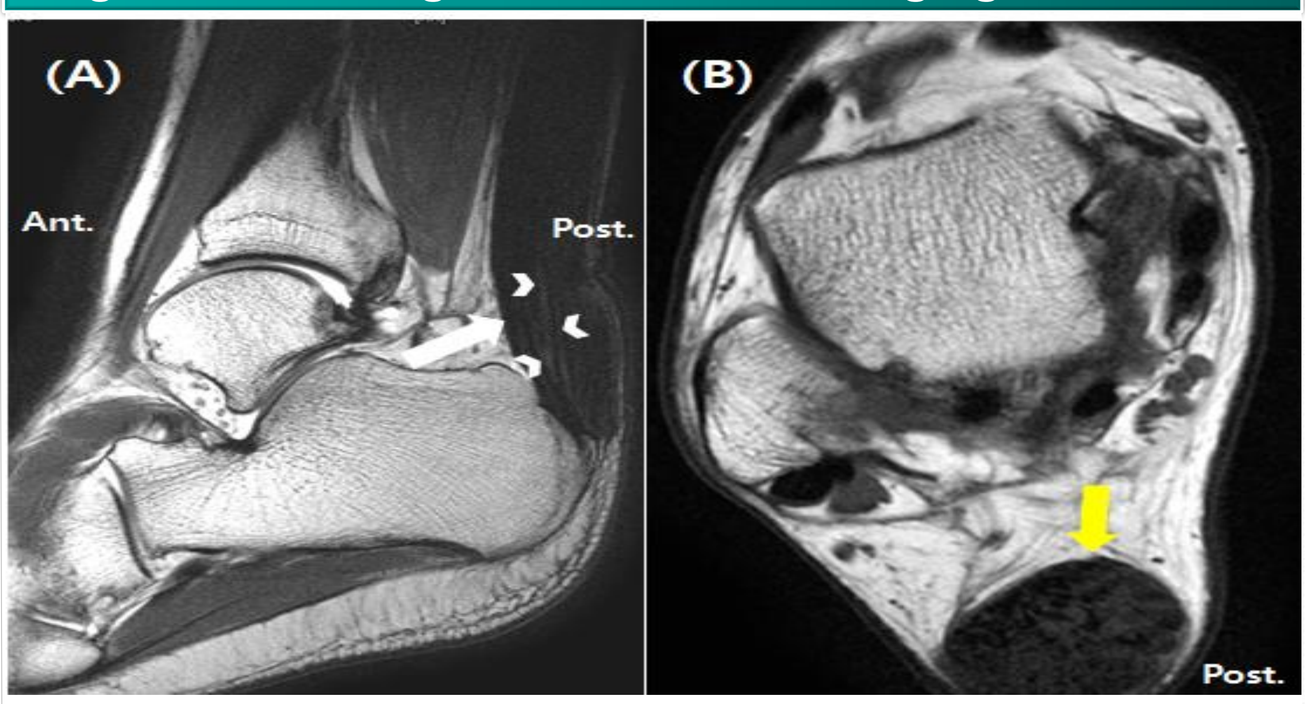
Abbreviations: MAS; Modified Ashworth scale, RAM; Rapid alternating movement

Figure 1. The Achilles tendon and Rt. knee of the patient



(A) Both Achilles tendon xanthomas (white arrow) and
(B) Xanthoma on right knee area (black arrow).

Figure 2. The magnetic resonance imaging of Rt. Ankle



Right ankle magnetic resonance imaging (MRI) of the patient with marked swelling of the Achilles tendon.
(Ant.: anterior, Post: posterior)

(A) T2 weighted sagittal plane demonstrated diffuse thickening (white arrow) and a reticulate pattern of the Achilles tendon (white arrowhead), showing the Achilles tendon xanthoma.
(B) Axial T1 weighted image demonstrated a thickening and heterogeneous signal of the Achilles tendon, with loss of its normal anterior concavity (yellow arrow).

Conclusion

- This case highlights **the importance of considering CTX** as a potential cause in patients **presenting with young adult-onset, progressive gait disturbance and spasticity.**
- Although CTX is rare, **early administration of chenodeoxycholic acid** could **slow down the progression** of **neurological dysfunction.**
- Therefore, it is crucial to suspect and confirm **the presence of tendon xanthoma**. When these signs are present, **CYP27A1 genetic testing** should be performed