
Hirayama’s disease
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- **Keizo Hirayama** is a neurologist from Chiba University in Japan
- In 1959, Hirayama, with two colleagues, reported 12 patients with :

  - predominantly unilateral **weakness** of the fingers and hand

  - **atrophy** of the hand and forearm

  which didn't fit with ALS or spinal muscular atrophy
- Largest series were reported in Asian countries :

  - **Japan** *(330 cases, Tashiro et al, 2006)*

  - **Taiwan** *(40 cases, Huang et al, 2008)*

  - Singapore, India, Malaysia, Sri Lanka, Hong Kong

- Cases have also been described in western countries :

  - France, Germany, Holland, UK, Denmark, Poland, Australia, USA, Canada

- Hirayama's disease is also known as : monomelic amyotrophy and

  Juvenile

  Muscular

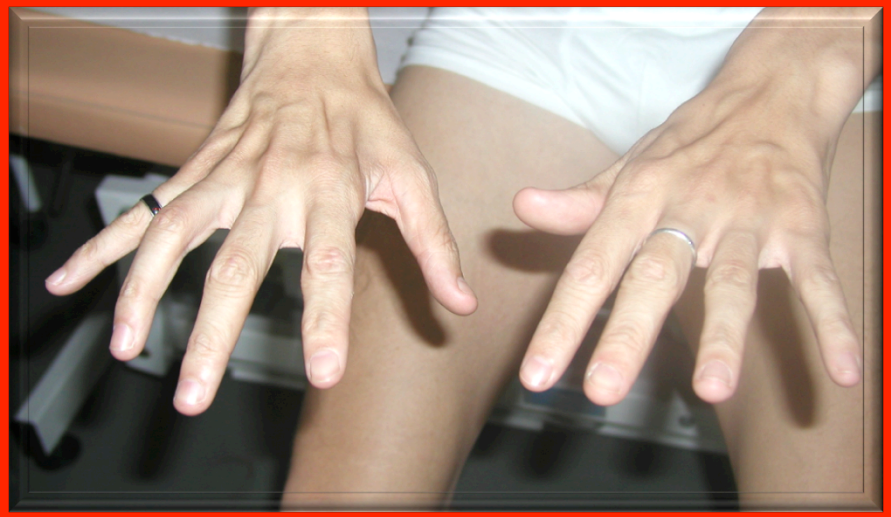
  Atrophy of the

  Distal

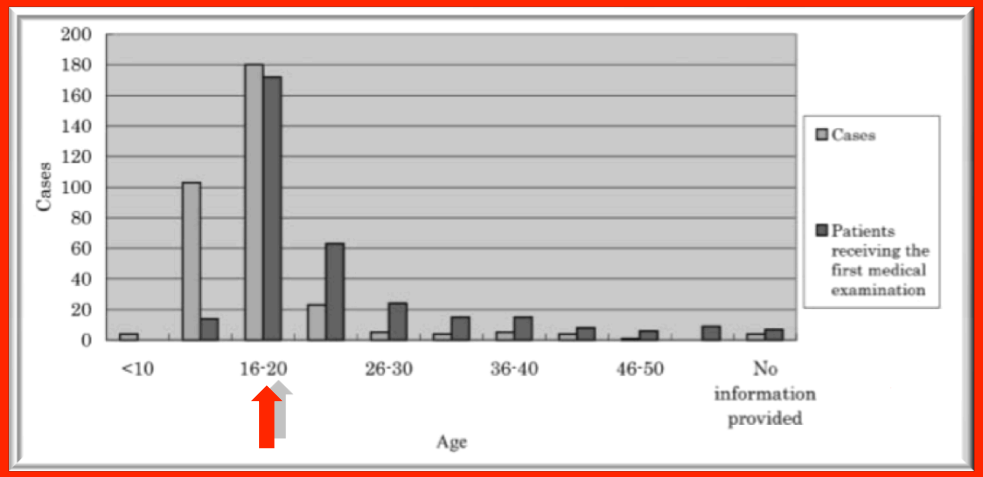
  Upper

  Extremity

JMADUE

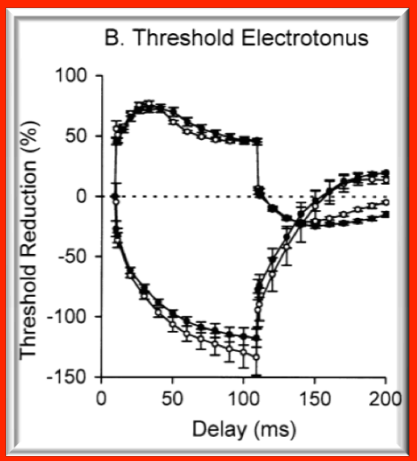


- The disease develops in young persons, mostly in **males** (89 %), between **11** and **25** years, often slender sportsman (football, rugby)
- For females, onset is slightly older (mean 19,3 years) than for males (mean 17,6 years)
- Almost all cases are **sporadic**
- Familial cases are quite rare : some pairs of brothers and one family with a father and son
- HD seems to be **not linked** to SOD1, SMN1, SMN2, GARS and androgen receptor genes

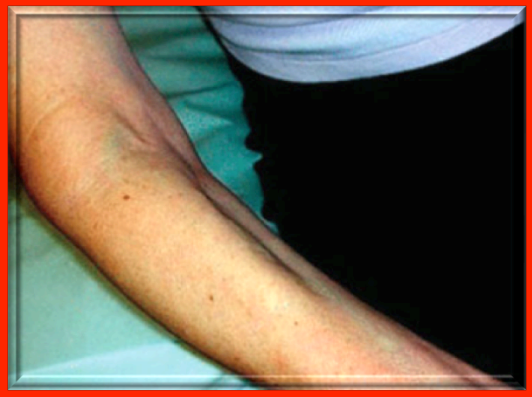


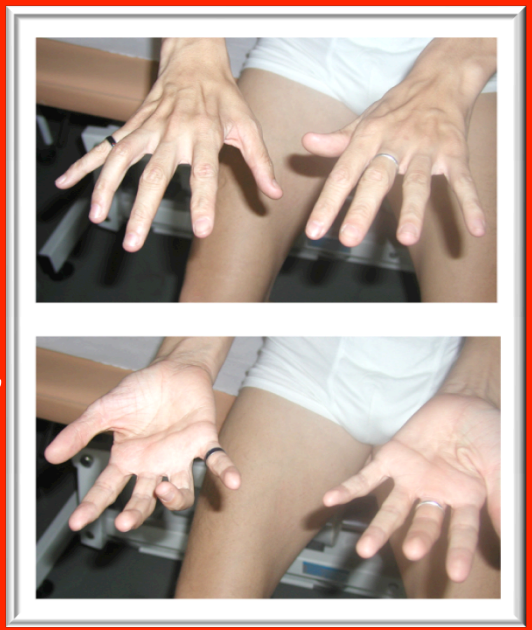
- The onset is very **insidious**, without precipitant toxic history, infection or trauma
- Many patients (97 %) report that weakness easily **worsens in a** somewhat **cold environment**, and improves in a warm one
- The patients often first notice their disease during the winter
- However, **cold paresis** is also reported in other diseases (ALS)
- Cold paresis might be due to a dysfunction of sodium and potassium axonal channels

(Sawai et al, 2011)



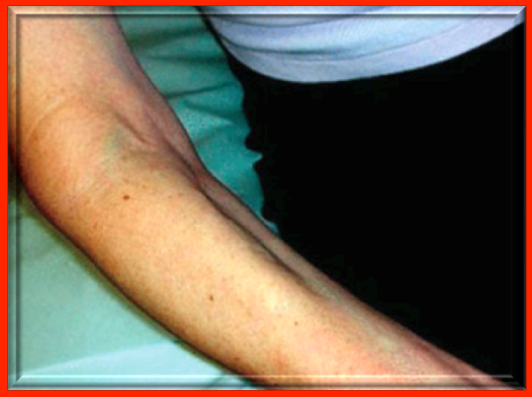
- Atrophy and weakness of muscles is confined to the hand and forearm (**C7-T1** segments)
- Brachioradialis muscle is spared = **oblique amyotrophy**
- **Ulnar** territory is **more affected than median** one
- The **right side** is more often affected, regardless of handedness
- The amyotrophy is **unilateral** in most patients (72 %), asymmetrically bilateral in some (25 %) and rarely symmetric (3 %)

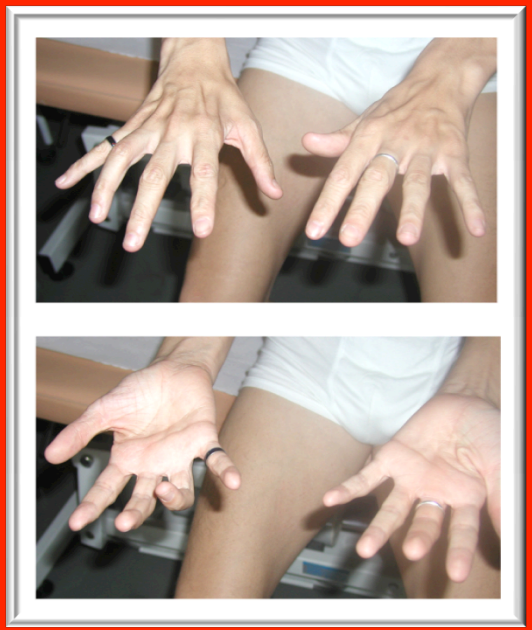




CLINICAL FEATURES : ***oblique amyotrophy and unilateral predominance***

- Fasciculations are rare
- Moderate extension of the fingers, usually produces fine, fast, irregular and non-synchronous **tremulous movements**
- Simultaneously, irregular, recurrent, short **twitchings on contraction** are observed in the dorsolateral portion of the forearm
- Slight and inconstant autonomic disturbances : cyanosis, livedo reticularis, hyperhidrosis, Horner's syndrome





- Usually, careful examination **does not reveal sensory impairment**
- Occasional numb sensation or slight hypoesthesia in a localized area on the dorsum of the hand are reported
- **Stretch reflexes are within normal range** or reduced in the upper limbs (sometimes with hyperreflexia in the lower limbs, babinski sign is reported in very few cases)
- **Absence of central motor deficit, ocular dysfunction and urinary disturbance**

- The disease progression is arrested within 3 years in 70 % of cases and within **6 years in 9O %** of cases
- The disease **stops** progressing **before age 25 years** in the majority of cases

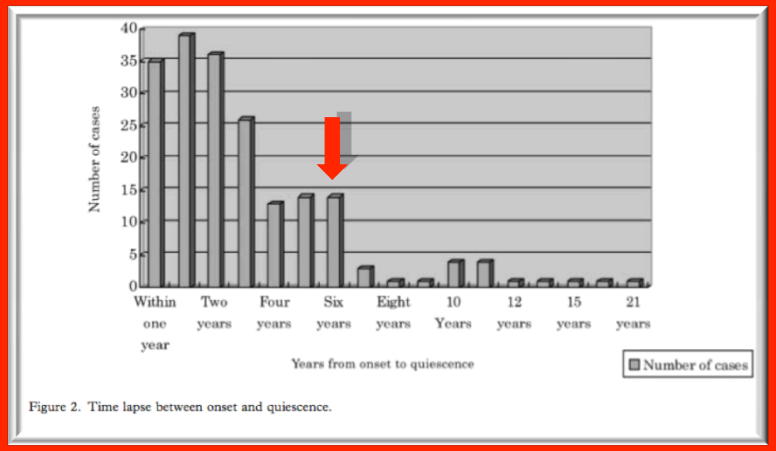
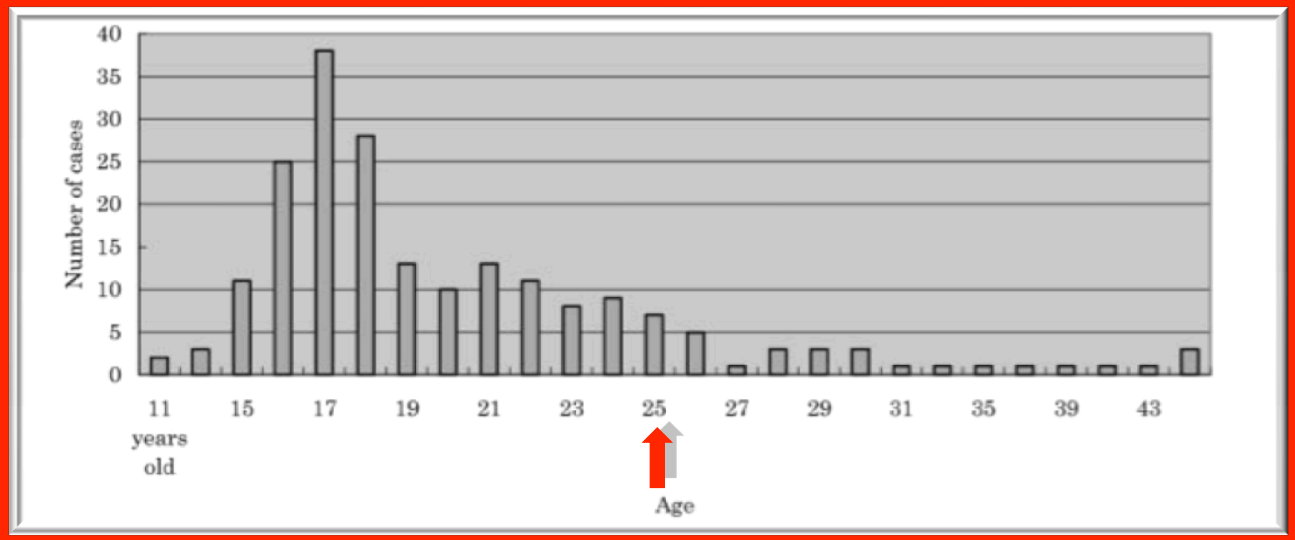
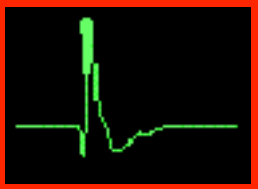


Figure 2. Time lapse between onset and quiescence.





- **Sensory neurography is normal**
- >< Carpal tunnel syndrome

  Ulnar neuropathy at the elbow (or at the wrist)

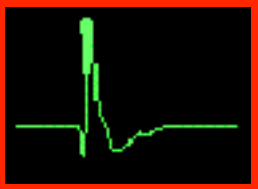
  TOS

  Polyneuropathy

  Mononeuritis multiplex

  Kennedy's disease

•Ulnar nerve
•Median nerve
•Medial antebrachial cutaneous nerve



- Ulnar territory is more affected than median territory
- **Ulnar/median CMAP amplitude ratio** *(Lyu et al 2011)*

[0.6 – 1.7] : normal subjects

> 1.7 : ALS, TOS

< 0.6 : Hirayama's disease

Cervical spondylotic amyotrophy

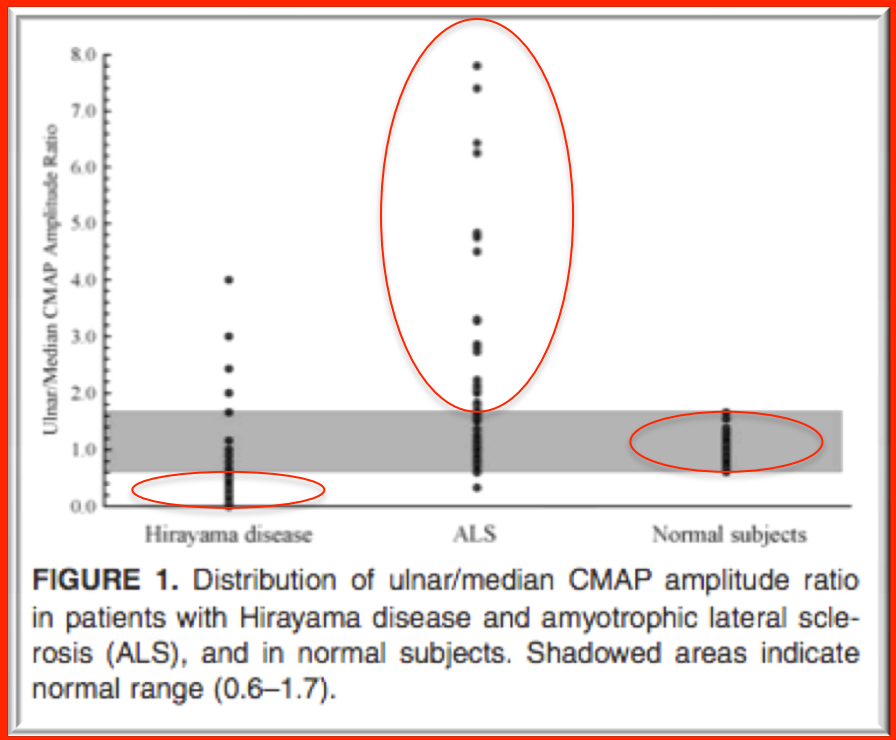
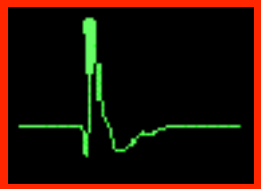
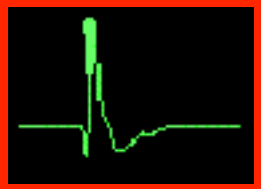


FIGURE 1. Distribution of ulnar/median CMAP amplitude ratio in patients with Hirayama disease and amyotrophic lateral sclerosis (ALS), and in normal subjects. Shadowed areas indicate normal range (0.6–1.7).



- Motor distal latency and **conduction velocity are normal** or slightly prolonged or mildly slow (related to the loss of fast conducting axons)
- **Absence of** conduction block and temporal dispersion
- >< CIDP
  - Multifocal motor neuropathy
  - Hereditary demyelinating neuropathy

•Ulnar nerve
•Median nerve

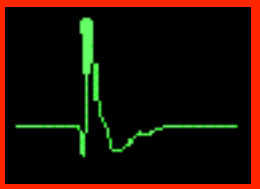


- Needle EMG shows chronic denervation in the **C7, C8, and T1 myotomes**
- The **ulnar motor fibers** are more affected than the median ones
- **Subclinical involvement** of C5 and C6 myotomes and of the unaffected upper limb is **common**
- EMG of the lower limbs shows a normal pattern

•FDI/ADM
•APB
•EDC
•Wrist flexors
•Wrist extensors
•Triceps
•Biceps
•Deltoid

+++

N/+



- Median and ulnar **N9**, **N13**, and N20 latency and amplitudes are usually **normal** in neutral and neck flexion *(Misra et al, 2006)*

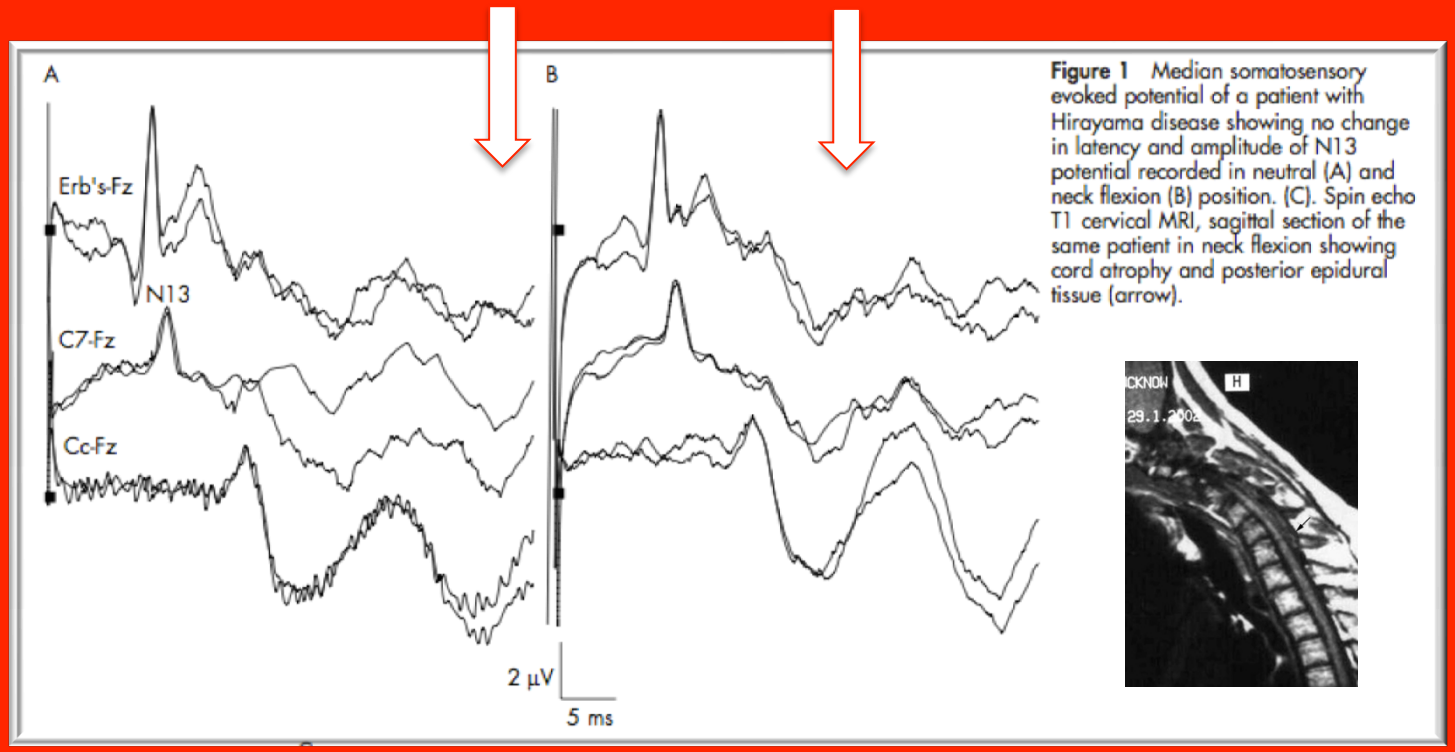
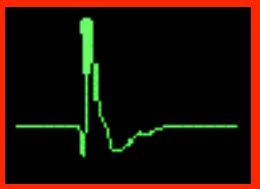
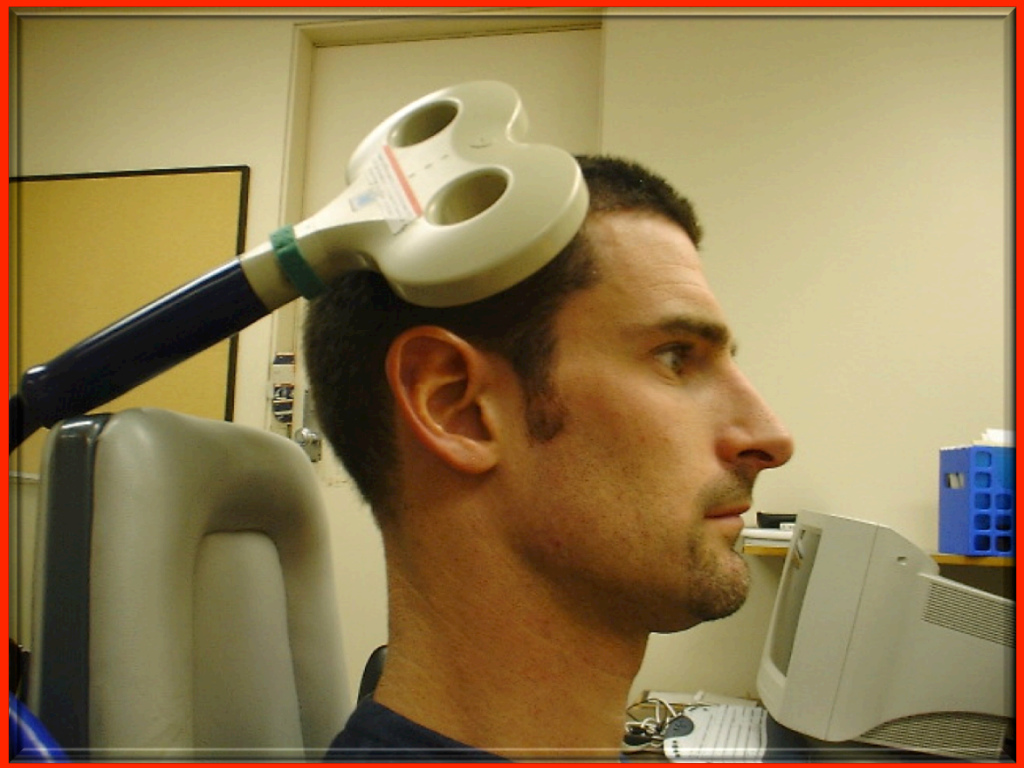


Figure 1 Median somatosensory evoked potential of a patient with Hirayama disease showing no change in latency and amplitude of N13 potential recorded in neutral (A) and neck flexion (B) position. (C). Spin echo T1 cervical MRI, sagittal section of the same patient in neck flexion showing cord atrophy and posterior epidural tissue (arrow).

- Attenuation of both the EP potentials and the N13 spinal responses, particularly during neck flexion, are sometimes reported *(Restuccia et al, 2003)*

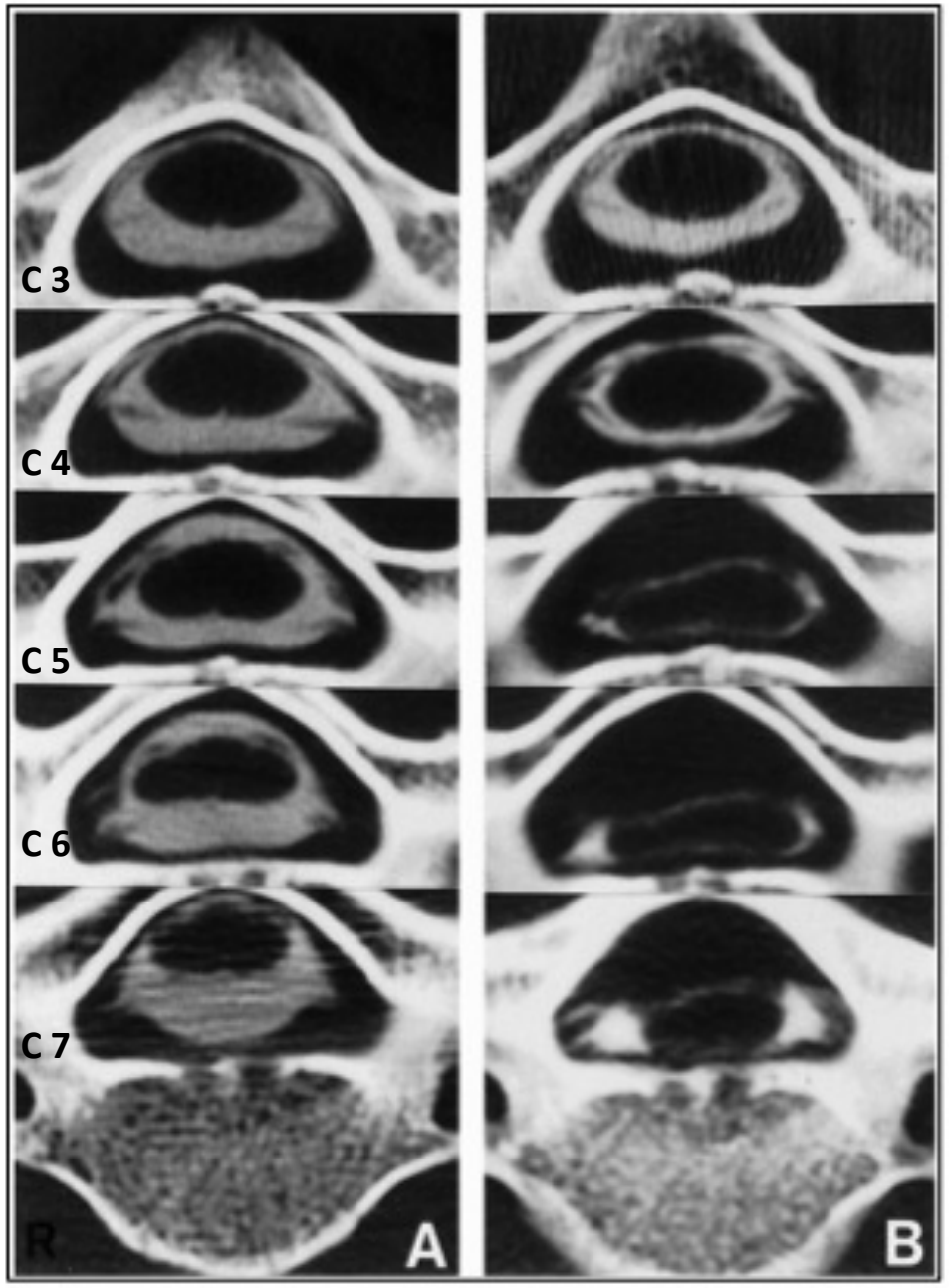




- **MEP are normal** in latency and in amplitude
- CMCT between cortex and C8-T1 is sometimes marginally prolonged

- (A) There is mild antero-posterior flattening of the spinal cord at the C6 vertebral level in a neutral neck position
- (B) Full neck flexion induces **forward displacement of the dural sac** and remarkable **flattening of the spinal cord** at the C5-7 vertebral levels

(Hirayama et Tokumaru, 2000)



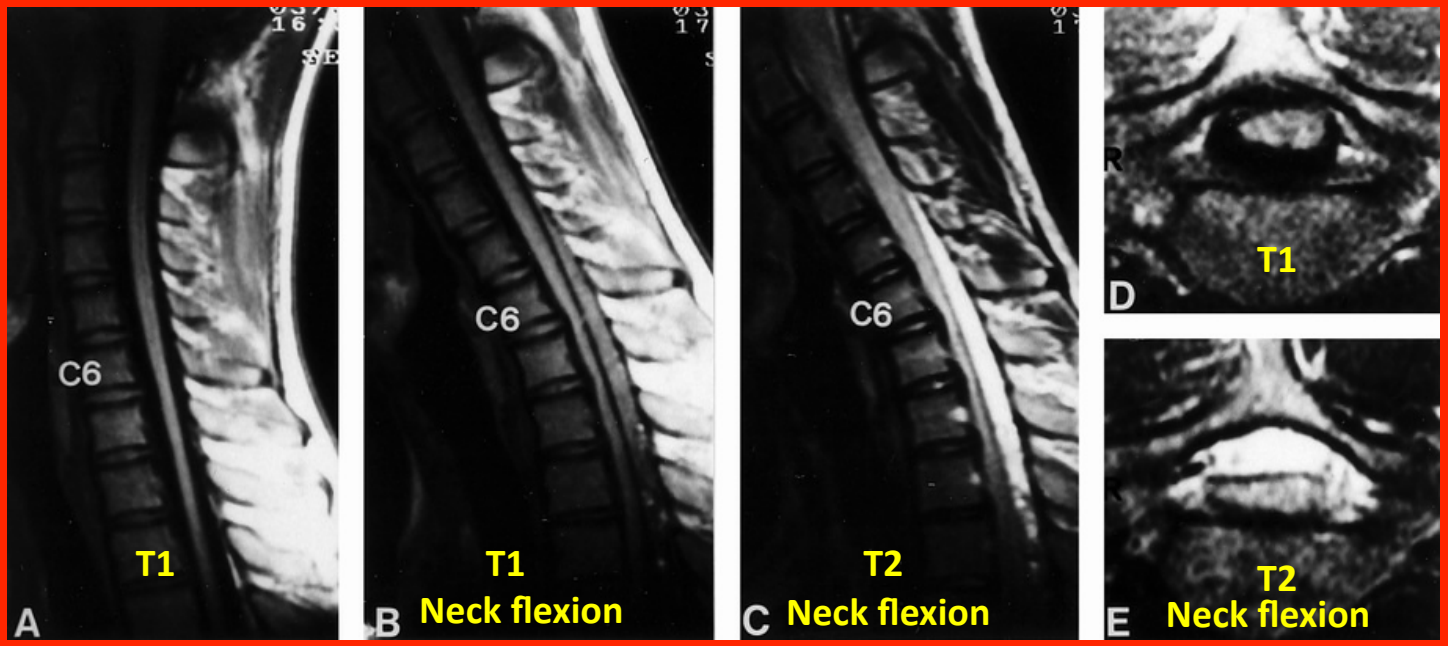
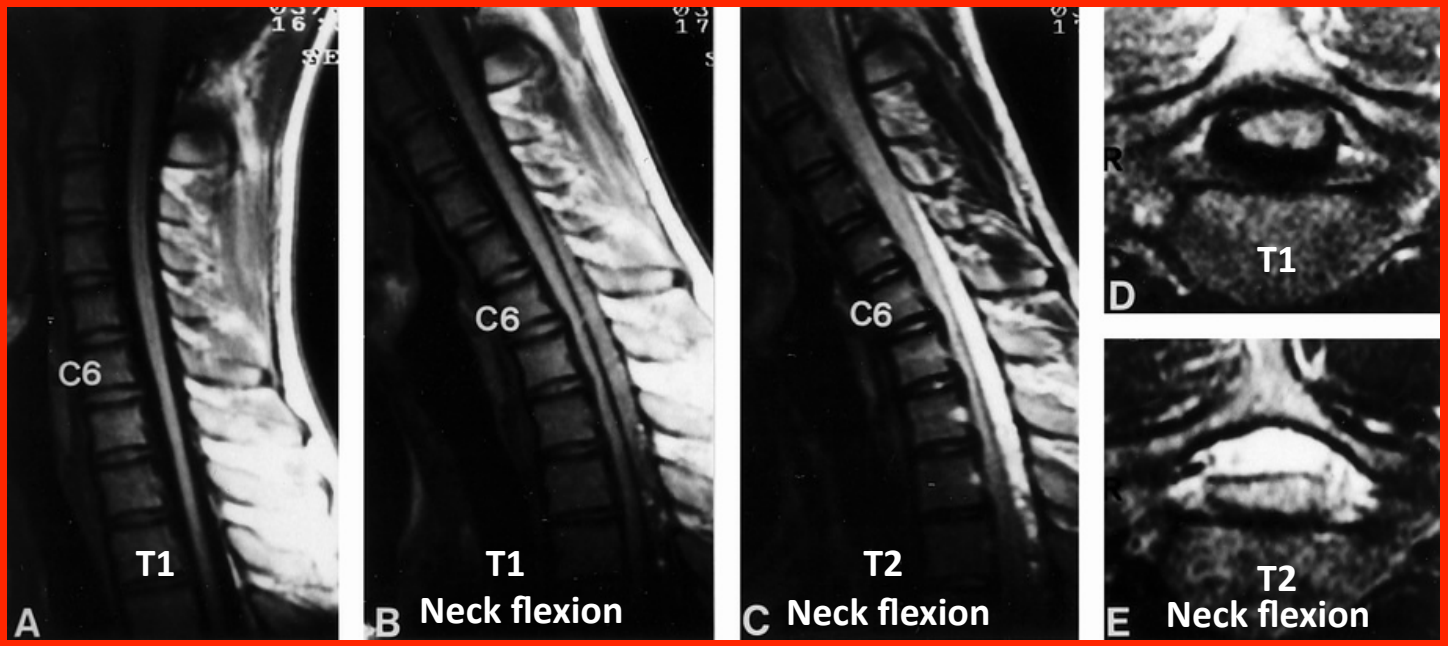


Table V. Abnormal findings of cervical cord and dura mater on neuroradiological examinations.

		Myelography (185 cases)	CT after myelography (171cases)	MRI (sagittal section) (229 cases)	MRI (horizontal section) (229 cases)
Atrophy of cervical cord	A	65%	83%	65%	75%
Flattening of cervical cord	D	72	86	76	77
Forward displacement of cervical cord	E	86	88	81	81
Forward displacement of posterior wall of dural tube	B	74	75	68	69
Expansion of posterior extradural space	C		-	73	



- There is no abnormal intrinsic cord signal
- **Full neuroradiological signs** are observed when disease duration **> 18 months** *(Fu et al, 2008)*
- In patients with a **disease duration more than 10 years**, dynamic changes disappear, but **atrophy** of the lower cervical cord is still present

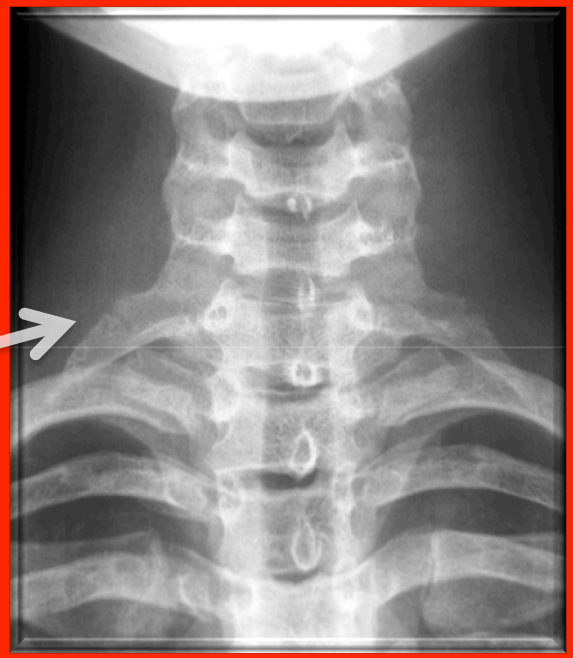
- Clinical and electrophysiological data are in favour of a proximal neuropathy as a **chronic axonal polyradiculopathy**, a **motor neuronopathy** or a **pure motor neuropathy**
- Abnormal sensory neurography :

  - **TOS** : medial antebrachial cutaneous nerve,

  ulnar sensory nerve,

  motor median nerve > motor ulnar nerve

  (**Ulnar/median CMAP amplitude ratio > 1.7**)

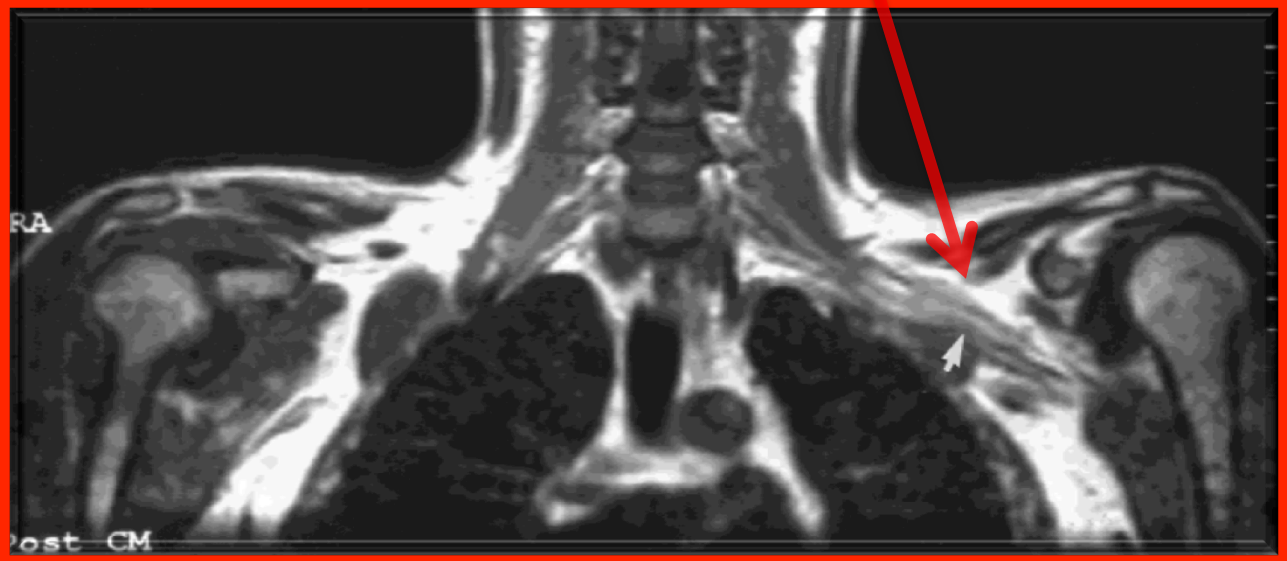


  - Lower trunk of brachial plexus : **perineurioma** (localized hypertrophic neuropathy)

- Abnormal imagery :

  - **TOS** : **cervical X-ray** (cervical cost, C7 apophysomegaly)

  - **brachial plexus benign tumor** (perineurioma) : **MRI**



  - **Syringomyelia** : **MRI**

  - **Cervical myelopathy** associated with spondylosis or tumor : **MRI**

- Normal sensory neurography and imagery :

  - **ALS** : fascicualtions (thoracic region, lower limbs), bulbar or pseudo-bulbar signs, amyotrophy and weakness beyond C7-T1 myotomes, central motor impairment (**MEP**), subacute and progressive course (> 3 years)

  -**Acute anterior poliomyelitis** : acute course, fever

  - **CIDP** and **multifocal motor neuropathy** with or without conduction block (**TST**, *Magistris et al, 1999*)

- If any atypical sign : **hematological and immunological assessment**, **PET-scan**

- Chronic segmental **spinal muscular atrophy** (O'Sullivan-McLeod syndrome) :

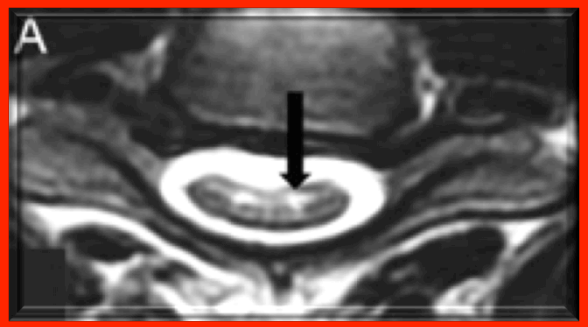
  - more progressive course

  - two genes are identified : GARS and BSCL2

- Partial **spinal anterior artery syndrome**

  - subacute course

  - T2 hyperintense cord signal in anterior horn (**snake eyes** in MRI transversal plane)



- Chronic progressive **degenerative disease** of cervical motoneurons *(Robberecht et al, 1997 ; Schröder et al, 1999)*, but :

  - the disease progression is arrested within 3-6 years in 90 % of cases

- **Flexion myelopathy** *(Hirayama and co-authors)*

  - the *primum movens* : might be a disproportionate growth between the vertebral column and the contents of the spinal cord

  - on neck flexion, the tight dural sac cannot compensate for the increased length of the posterior wall, which causes anterior shifting of the posterior dural wall and consequent compression of the cord =>

  - an increased intramedullary pressure, resulting in microcirculatory disturbance in the **anterior horn** (the most vulnerable structure to **ischemia**)

- Based on a flexion myelopathy mechanism : **cervical collar therapy**

  - improvement is expected in patients who have shorter of illness (< 2.5 years) and have mild cord atrophy in a neutral neck position

  - early diagnosis and therapeutic intervention may minimize the functional disability of young patients

- **Surgery** : cervical decompression and fusion,vertebrectomy, duraplasty

  - cervical cord compression in a neutral neck position

  - abnormal intrinsic cord signal

  - impairment beyond anterior horns

- Hirayama's disease occurs almost exclusively in **males** of **15-25** years, often slender sportsman, and is not usually hereditary
- **Insidious onset** of **oblique amyotrophy**, **unilateral** in many cases **or asymmetric**, often associated with **cold paresis**
- **Muscular tremor**, in extensors of the wrist and the fingers, on moderate extension
- In general, absence of sensory disturbance, ocular dysfunction or urinary disturbance
- Progressive course and **arrest within 3 to 6 years** after onset

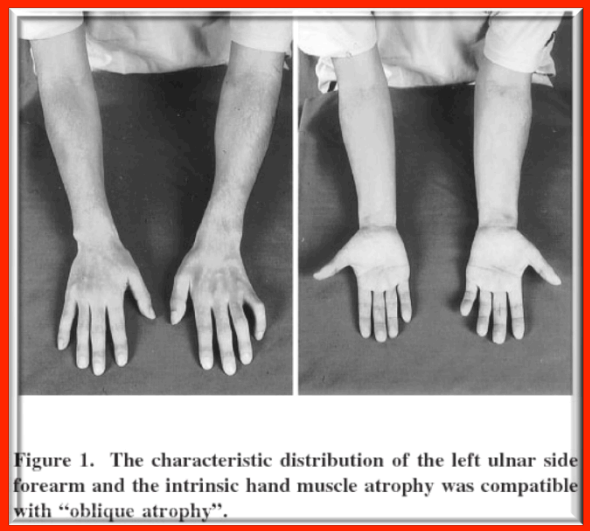
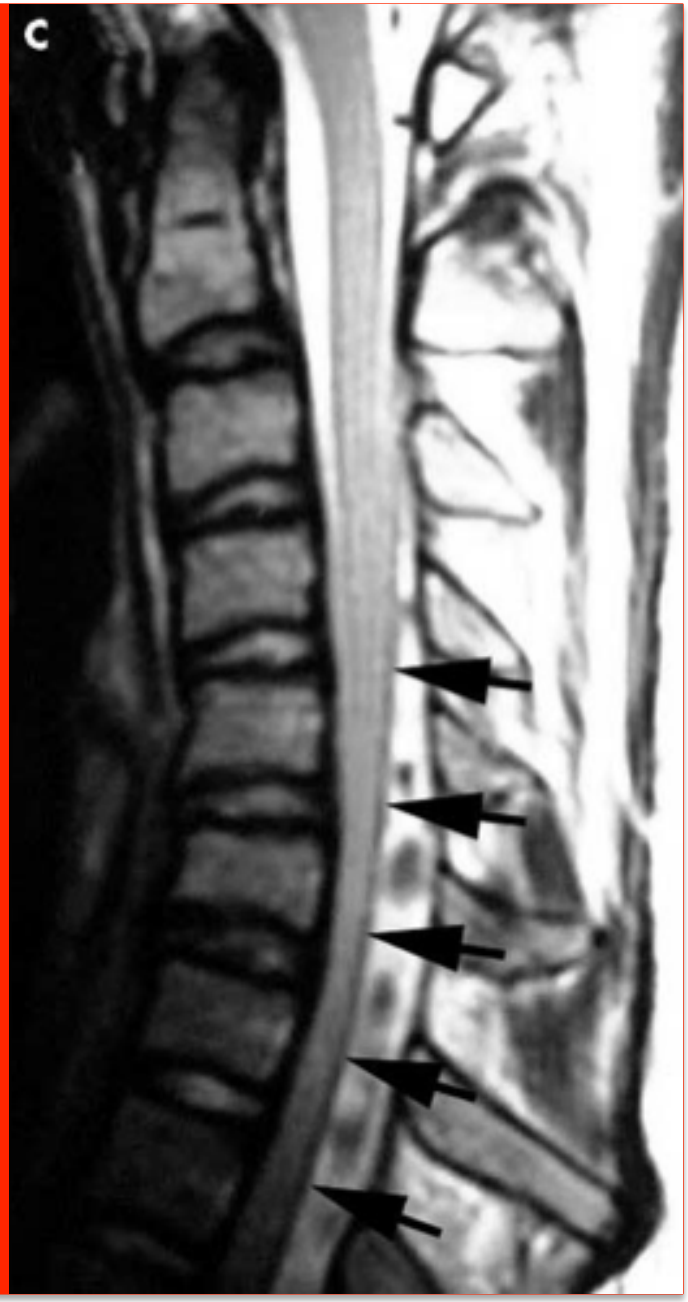


Figure 1. The characteristic distribution of the left ulnar side forearm and the intrinsic hand muscle atrophy was compatible with "oblique atrophy".

- **Neurogenic changes** in EMG, distributed mainly to **C7, C8 and T1** myotomes, **ulnar superior** median territories
- Localized and **asymmetrical atrophy of the spinal cord** at the lower cervical levels with **forward displacement of the posterior wall of the dural canal in neck flexion**

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