Parsonage-Turner syndrome

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Outline

- Definition of syndrome
- Symptoms
- Clinical findings
- ENMG
- Imaging
- Etiology
- Prognosis
- Treatment
- Cases

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THE LANCET] ORIGINAL ARTICLES [JUNE 26, 1948

NEURALGIC AMYOTROPHY
THE SHOULDER-GIRDLE SYNDROME

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A SYNDROME comprising pain and flaccid paralysis of the muscles round the shoulder girdle occurred fairly often during the war years 1941–45, though previously it had been rare. We observed 136 cases during neurological work in the Army in the United Kingdom and in India Command.

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Precipitating causes

Precipitating Cause	*Cases*	*Precipitating Cause*	*Cases*
Operations	12	*Infections*	71
Herniotomy	8	Malaria	16
Appendicectomy	1	Typhus and malaria	5
Varicocele	1	Typhus	4
Pilonidal cyst	1	Typhoid	1
Mastoid	1	Dysentery	5
Trauma	10	Smallpox	1
Gunshot wound of remote parts	5	Glandular fever	1
Minor local trauma	5	Rheumatic fever	1
Other conditions	5	Chest infections	9
Lumbar puncture	1	Septic infections	9
Air encephalogram	1	Minor fevers	11
Antisyphilitic treatment	2	Poliomyelitis	2
Severe exposure	1	Diphtheritic polyneuritis	6

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SUMMARY

A syndrome consisting in severe pain across the shoulder and upper arm, followed by atrophic paralysis of muscles round the shoulder girdle, is described.

On clinical grounds it is thought that the pathological process can involve one or more peripheral nerves, two or more spinal roots, or the spinal cord.

The condition appears to be a distinct clinical entity which became increasingly common during the war years.

A similar syndrome may occur some days after the injection of serum, and the two conditions are probably identical, though the ætiology is unknown.

The name "neuralgic amyotrophy" is suggested.

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Terminology

- **Neuralgic amyotrophy**
  - Most commonly used term today
  - 5% do not have any pain
  - Purely sensory nerves may be affected
- Plexus neuritis
  - Traditionally used in many countries
  - Affects also other structures
- Idiopathic brachial neuritis
- Multifocal multifascicular inflammatory and constrictive brachial neuritis
  - Often very focal
  - Fascicular entrapment (Vastamäki)
- **Parsonage – Turner syndrome**

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Classical PTS - Pain 1

- Acute onset with pain
- 95% onset with severe pain
  - NRS 7-9/10
- Often onset at night
- Initial pain usually a few weeks
  - 5% 24 hours
  - 10% > 2 months
- Weakness of muscles innervated by affected nerve
- Sensory abnormalities

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Classical PTS - Pain 2

- Pain is constant, not related to position
- Neurologic deficits become evident some time after onset of pain
- Pain is often not in the same region as the neurological deficit

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Atypical PTS

- No pain
  - 5% without pain
- Onset with paresis followed by pain
  - 5 %

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PTS distribution

- Spinal nerves (nerve roots)
- Plexus brachialis
  - Upper trunk with long thoracic nerve 50%
  - Upper/middle without long thoracic 25%
  - All parts affected 14%
  - Middle trunk/posterior cord 6%
  - Lower plexus 3%
- Individual nerves originating from the plexus
  - Long thoracic nerve
  - Suprascapular nerve
  - Axillary nerve

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PTS distribution

- Individual nerve of branches in the arm
  - Anterior interosseus nerve
  - Posterior interosseus nerve
  - Lateral cutaneous of the forearm
  - Radial nerve sensory branch
  - Sometimes nerves to individual muscles
- Cervical plexus
  - Phrenic nerve (10%)
- Cranial nerves
  - XI (Accessory nerve)
  - XII (Hypoglossal nerve)
  - IX (Glossopharyngeal nerve)
  - VIII (Vestibular neuritis?)
  - Bell's palsy??????
- ***Legs - sometimes***

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PTS distribution

- Unilateral 75%
- Bilateral 25%
- Dominant > non-dominant arm
- Mononeuropathies
- Often multifocal
  - *The lesions appear sequentially at different times*

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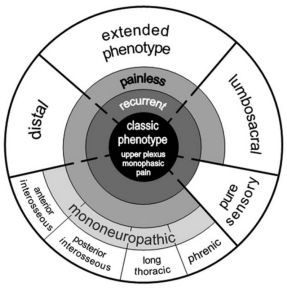
Van Alfen. Nat Rev Neurol 2011;7:315-322



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PTS incidence: PLOS ONE 2015; May:1-9

RESEARCH ARTICLE

Incidence of Neuralgic Amyotrophy (Parsonage Turner Syndrome) in a Primary Care Setting - A Prospective Cohort Study

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Incidence in primary care 1/1000/year

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PTS age and gender

- Children and adults
  - Mean age of onset 40 years
  - Range 10-90 years
- Male : female = 2:1
- 10% have a family history
- Lean > obese

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Recurrence

- 20% one recurrence
- 5 % two recurrences
- 4 % three recurrences
- 1 % four or more recurrences

30% will recur!

Van Alfen N, van Engelen BGM. The clinical spectrum of neuralgic amyotrophy in 246 cases. Brain 2006;129:438-450

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Nerve biopsy findings

- Epineural perivascular mononuclear T-cell infiltration
- Active multifocal axonal degeneration without blood vessel wall inflammation or necrosis
- Perineural thickening

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Predisposing factors PTS

- Infection
  - 10% have hepatitis E
  - Coxacie A2
  - Covid 19 not more prone than other virus infections
- Surgery
- Childbirth
- Unusual physical activity
- Vaccination
  - (Covid 19 vaccines not more prone than other vaccines)
- Trauma
- Onset usually within within 2 weeks of predisposing event
- May start within hours of predisposing events
- Diabetes not predisposing factor!!!!
- Lean subjects

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Pathophysiology of PTS

- ***Immune mediated***
- Genetic predisposition
  - Hereditary neuralgic amyotrophy (HNA – SEPT9 mutation)
  - Other yet unknown mutations
  - Tendency for recurrent episodes
- Mechanical factors
  - Lesions often around joints
  - Preceding repetitive physical activity
- *Organ specific immune mediated disorder*

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ULTRASONOGRAPHIC IDENTIFICATION OF NERVE PATHOLOGY IN NEURALGIC AMYOTROPHY: ENLARGEMENT, CONSTRICTION, FASCICULAR ENTWINEMENT, AND TORSION

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Accepted 10 February 2015

ABSTRACT: *Introduction:* The aim of this study was to characterize the ultrasonographic findings on nerves in neuralgic amyotrophy. *Methods:* Fourteen patients with neuralgic amyotrophy were examined using high-resolution ultrasound. *Results:* Four types of abnormalities were found: (1) focal or diffuse nerve/fascicle enlargement (57%); (2) incomplete nerve constriction (36%); (3) complete nerve constriction with torsion (50%; hourglass-like appearance); and (4) fascicular entwinement (28%). Torsions were confirmed intraoperatively and were seen on the radial nerve in 85% of patients. A significant correlation was found between no spontaneous recovery of nerve function and constriction/torsion/fascicular entwinement ($P = 0.007$). *Conclusion:* Ultrasonographic nerve pathology in neuralgic amyotrophy varies in order of severity from nerve enlargement to constriction to nerve torsion, with treatment ranging from conservative to surgical. We postulate that the constriction caused by inflammation is the precursor of torsion and that development of nerve torsion is facilitated by the rotational movements of limbs.

Muscle Nerve **52**: 503–511, 2015

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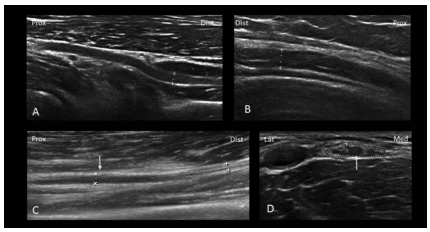
Nerves with edema



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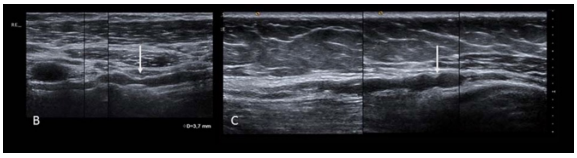
Hour glass constriction



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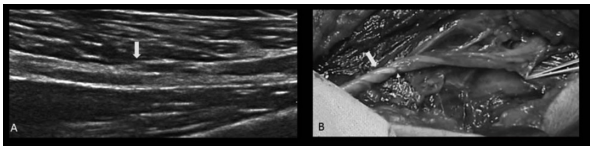
Entwinement



Ultrasound Intraoperative

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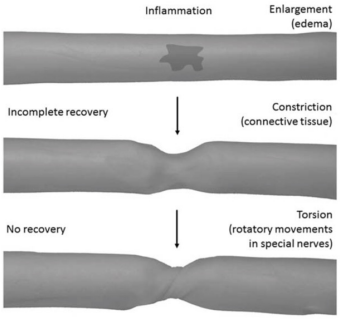

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Typical nerves affected

- Spinal nerves (= radiculopathy)
- Plexus brachialis
- N.thoracicus longus
- N.suprascapularis
- N.interosseus anterior
- N.interosseus posterior
- N.axillaris
- Plexus lumbalis
- N.phrenicus
- N.accessorius
- ……..

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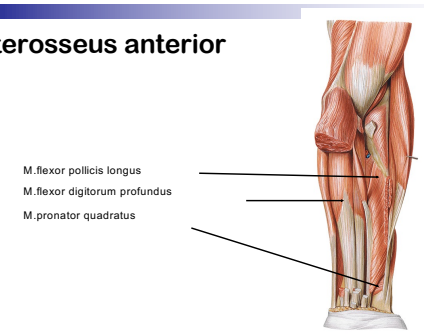
N.interosseus anterior



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N.anterior interosseus

- Severe pain in the forearm
  - 2 days to 2 months
- Distal phalanx of thumb and forefinger flexion weak
- Variable recovery
- Parsonage Turner syndrome (neuralgic amyotrophy)
- Anterior interosseus syndrome not an entrapment

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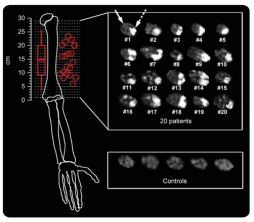
Anterior interosseus neuropathy



Spatial (red circles, upper left) and statistical (red box-and-whisker plot, upper left) distributions of predominant individual lesion sites and array of individual median nerve cross-sectional magnetic resonance neurography images (upper right) for the patient group (n = 20, numbered in accordance with table e-1). Localization of individual lesion sites is given as distance in cm from humeroradial joint space (at 0 cm). Differences in individual arm lengths were not corrected for. In all patients, strongly increased T2 signal (bright) was found within a group of fascicles whereas other fascicles were spared, indicated by dashed (lesion) and solid (normal fascicles) white arrows in patient 1. Nerve T2 signal was normal in controls (lower right showing 5 representative out of 20 control subjects).

Pham et al. Anterior interosseous nerve syndrome. Neurology® 2014;82:598–606

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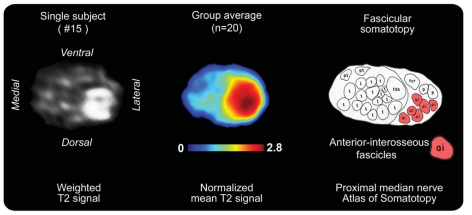

On the left, the T2-weighted source image of the median nerve of patient 15 is shown for the site of predominant lesion focus (17.1 cm proximal to humeroradial joint). Anatomical orientation is given by labeling ventral/dorsal/medial/lateral contours. In the middle, a spatial map of the patient group mean normalized T2 signal is shown. This map was rendered after segmentation and intersubject image registration. On the right is a somatotopic/topographic internal map of fascicles of the median nerve trunk. This schematic drawing was obtained by Jabaley et al.[31] from tracing extraneural median nerve branches from distally to intraneural proximal fascicles within the median nerve trunk on 20-μm-thick cuts after intraneural microsurgical dissection and histologic photographing (modified from Jabaley et al.[31] with permission). On this map, the red fascicles ("ai": anterior-interosseous) are in close spatial arrangement with the T2 lesion focus on individual (left) and group level (middle). This cross-sectional lesion area is at the dorsal and lateral/radial aspect of the median nerve at upper arm level with a mean distance of 14.6 ± 5.4 cm proximal to the humeroradial joint space.

Pham et al. Anterior interosseous nerve syndrome. Neurology® 2014;82:598–606

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Posterior interosseous neuropathy

Supinator syndrome vs fascicular radial neuropathy

OPEN

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ABSTRACT

Objective: To investigate the spatial pattern of lesion dispersion in posterior interosseous neuropathy syndrome (PINS) by high-resolution magnetic resonance neurography.

Methods: This prospective study was approved by the local ethics committee and written informed consent was obtained from all patients. In 19 patients with PINS and 20 healthy controls, a standardized magnetic resonance neurography protocol at 3-tesla was performed with coverage of the upper arm and elbow (T2-weighted fat-saturated: echo time/repetition time 52/7,020 milliseconds, in-plane resolution 0.27 × 0.27 mm²). Lesion classification of the radial nerve trunk and its deep branch (which becomes the posterior interosseous nerve) was performed by visual rating and additional quantitative analysis of normalized T2 signal of radial nerve voxels.

Results: Of 19 patients with PINS, only 3 (16%) had a focal neuropathy at the entry of the radial nerve deep branch into the supinator muscle at elbow/forearm level. The other 16 (84%) had proximal radial nerve lesions at the upper arm level with a predominant lesion focus 8.3 ± 4.6 cm proximal to the humeroradial joint. Most of these lesions (75%) followed a specific somatotopic pattern, involving only those fascicles that would form the posterior interosseous nerve more distally.

Conclusions: PINS is not necessarily caused by focal compression at the supinator muscle but is instead frequently a consequence of partial fascicular lesions of the radial nerve trunk at the upper arm level. Neuroimaging should be considered as a complementary diagnostic method in PINS. *Neurology®* 2016;87:1884–1891

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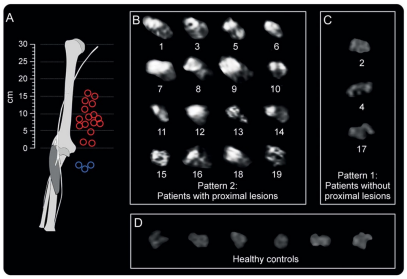
Posterior interosseous nerve fascicular lesion



T2-weighted turbo spin echo

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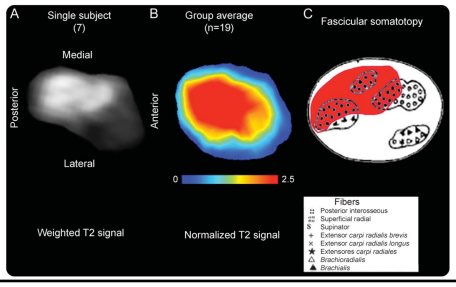
Somatotopic findings



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N.thoracicus longus

- Winging of the scapula
- Difficulty of abduction of the arm above the shoulder
- Slow recovery
  - axonal reinnervation starts at 6-8 months after onset
  - recovery completed at two years after onset

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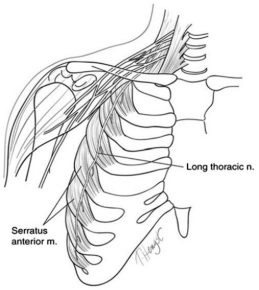
N.thoracicus longus



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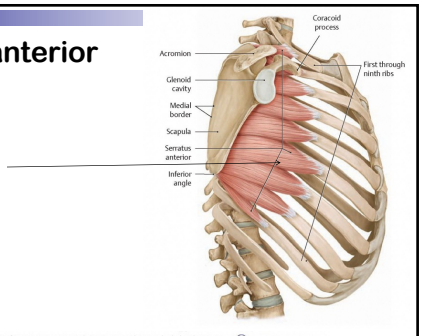
M.serratus anterior



Innervation: N.thoracicus longus
Myotomes: C5-7

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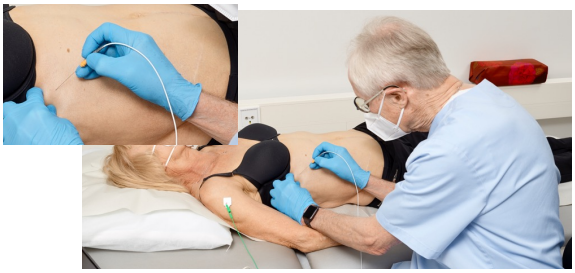
M.serratus anterior



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M.serratus anterior - activation

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Long thoracic nerve neuropathy on the right side
9/2009, onset after childbirth 7/2009

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Long thoracic nerve neuropathy on the right side
9/2009, onset after childbirth 7/2009

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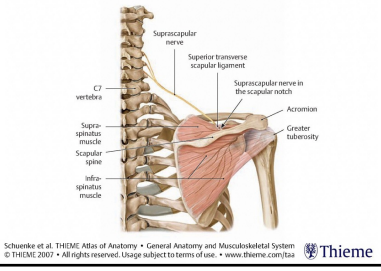
Suprascapular nerve



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N.suprascapularis

- Shoulder pain
- Weak upper arm outward rotation
- Weak shoulder abduction
- Atrophy of m.infraspinatus and m.supraspinatus

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Hereditary neuralgic amyotrophy
HNA

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Hereditary neuralgic amyotrophy (HNA)

- Genetically heterogeneous
- One form linked to chromosome 17q24
  - Gene codes septin 9 (SEPT9)
  - Septins are implicated in the formation of the cytosceleton, cell division and tumorgenesis
  - Missense mutations
  - Intragenic duplications
- Autosomal dominant inheritance
- Variable penetrance
- Onset often in early childhood

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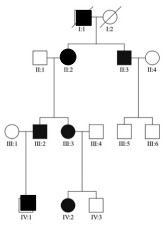
Pedigree of own HNA family



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HNA - Clinical features

- Onset usually in second to third decades
- Sometimes in the first decade
- Painful episodes of local nerve lesions
- Pain lasting a few days to a few weeks
- Often satisfactory recovery
- Repeated or severe attacks leave residual symptoms
- Penetrance high - 80%

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EMG findings in HNA

- In unaffected parts normal EMG and neurography
- Abnormalities only in affected nerves
- Different from HNPP (hereditary liability to pressure palsies)

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Diagnosis

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Diagnosis

- Clinical picture
- Symptoms
- Laboratory tests
- Imaging
- ENMG

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Laboratory tests

- SR, CRP normal
- Autoimmune antibodies normal
- Spinal fluid
  - Sometimes elevated proteins or lymphocyte counts
- If risk factors present
  - Borrelia
  - HIV

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Imaging

- MRI of the plexus
  - Abnormalities often seen
- Ultrasound
  - Very good in experienced hands

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Treatment

- Analgesia
  - NSAID, opioid if necessary
- Immunomodulation
  - No controlled studies
  - Should be started acutely at the onset! Within the first days!
    - Prednislone high dosage?
    - IVIg
  - Prevention of new episodes??
  - Shorter and better recovery times suggested in some uncontrolled studies
- Surgery
  - In severe cases with complete axonal involvement and torsion?
  - Future studies will soon show

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Gstoettner C, et al. J Neurol Neurosurg Psychiatry 2020;91:879–888.

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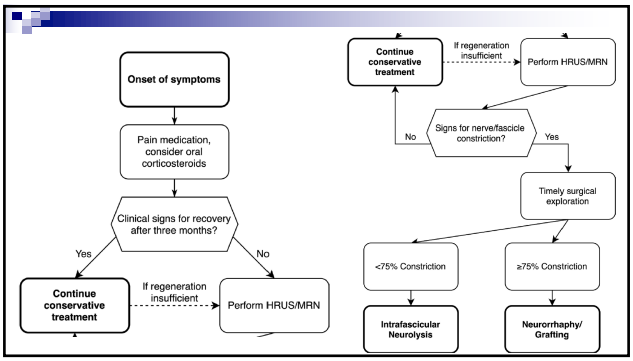

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Differential diagnosis

- Clinical picture usually quite clear
- If spinal nerve is affected cervical radiculopathy due to cervical disc herniation

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Outcome

- Nens Van Alfen
  - 10% full recovery
  - 60% will have some pain
  - 50% fatigue
  - 25% unable to work
- Cruz-Martinez A et al J Peripheral Nervous System 2002:7:198-204
  - Good outcome in the 22 out of 40 patients that were followed for 2 years
  - In 41 of 43 affected nerves good outcome

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Patient

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History

- 67-year-old woman
- 2 years ago, surgery for right breast cancer
- Postoperative radiation therapy right axilla
- Follow-ups showed no recurrent tumor
- 4 weeks prior to EMG severe pain in the right arm and paralysis of elbow and arm abduction

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Clinical findings

- Shoulder and elbow muscles weak
- Distal hand muscles good strength
- Loss of sensation over the upper arm

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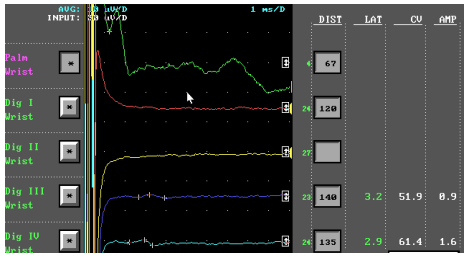
N.medianus - sensory neurography



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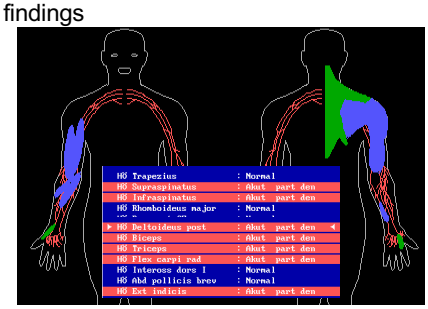
EMG findings



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Conclusion

- Severe, acute upper and middle trunk lesion
- Acute onset with sever pain suggests Parsonage-Turner syndrome

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Follow-up

- Pain subsided in a few weeks
- Follow-up at oncology department did not show metastatic lesions
- Muscle strength recovered slowly at 4 months after onset of symptoms

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Patient 2

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50 year old male

- Type 2 diabetes for 7 years
- Ten years ago, an episode of pain first in in the right shoulder and then in a few days later in the left shoulder lasting for a few weeks. Not investigated at that time.
- Two months prior to EMG TBE vaccination
- One-week after TBE vaccination pain in the right shoulder at night (VAS7/10)
  - Weakness of right arm and shortness of breath
- One-week later pain in the left shoulder
  - Weakness of external rotation and abduction of upper arm

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50 year old male

- Consulted a private neurologist
  - No breathing sounds on right ride
  - Chest X-ray showed elevation of right diaphragm
  - Refers patient to department of lung medicine

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50 year old male

- Examined at the department of lung medicine
- No cause for the problem found
- Referred for neurological consultation
- Before consultation neurologist refers patient for EMG
  - Neuromuscular disorder?

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Clinical findings

- Obese patient, BMI 34
- Right triceps reflex -, other tendon refexes normal bilaterally
- Weakness of right elbow extension
- Weakness of left upper arm external rotation and abduction

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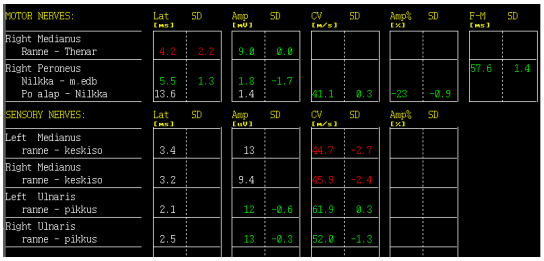
Neurography



MOTOR NERVES:	Lat (ms)	SD	Amp (mV)	SD	CV (m/s)	SD	Amp% (%)	SD	F-M (ms)	SD
Right Medianus Ranne – Thenar	4.2	2.2	9.0	0.0						
Right Peroneus Nilkka – m.edb	5.5	1.3	1.8	-1.7					57.6	1.4
Po alap – Nilkka	13.6		1.4		41.1	0.3	-23	-0.9		
SENSORY NERVES:	**Lat (ms)**	**SD**	**Amp (uV)**	**SD**	**CV (m/s)**	**SD**	**Amp% (%)**	**SD**		
Left Medianus ranne – keskiso	3.4		13		44.7	-2.7				
Right Medianus ranne – keskiso	3.2		9.4		45.9	-2.4				
Left Ulnaris ranne – pikkus	2.1		12	-0.6	61.9	0.3				
Right Ulnaris ranne – pikkus	2.5		13	-0.3	52.0	-1.3				

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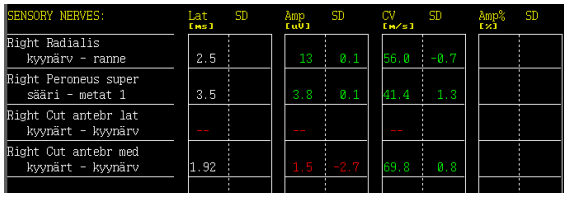
Neurography



SENSORY NERVES:	Lat (ms)	SD	Amp (uV)	SD	CV (m/s)	SD	Amp% (%)	SD
Right Radialis kyynärv – ranne	2.5		13	0.1	56.0	-0.7		
Right Peroneus super sääri – metat 1	3.5		3.8	0.1	41.4	1.3		
Right Cut antebr lat kyynärt – kyynärv	--		--		--			
Right Cut antebr med kyynärt – kyynärv	1.92		1.5	-2.7	69.8	0.8		

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EMG findings – left side

Muscle	Fibrillations	MUP amplitude	Interference pattern	Interpretation
Trapezius				Normal
Deltoideus		⬆	⬇	Slight inactive neurogenic
Biceps brachii		⬆	⬇	Slight inactive neurogenic
Triceps				Normal
Extensor indics				Normal
Flexor carpi radialis				Normal
Interosseus dors 1				Normal
Pectoralis major				Normal
Supraspintus	10/10		⬇⬇⬇	Severe acute neurogenic
Infraspinatus	10/10		⬇⬇⬇	Severe acute neurogenic

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EMG findings – right side

Muscle	Fibrillations	MUP amplitude	Interference pattern	Interpretation
Trapezius				Normal
Deltoideus		⬆	⬇	Slight inactive neurogenic
Biceps brachii		⬆	⬇	Slight inactive neurogenic
Triceps	6/10		⬇⬇	Moderate acute
Extensor indics				Normal
Flexor carpi radialis	8/10		⬇⬇	Moderate acute
Interosseus dors 1				Normal
Diaphragm	10/10		0	Severe acute neurogenic
Vastus lateralis				Normal
Tibialis anterior				Normal

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EMG summary

- Moderate acute right C7 spinal nerve neuropathy
- Severe acute left suprascapular nerve neuropathy
- Severe involvement of the right phrenic nerve
- Bilaterally a mild old upper plexus lesion
- Bilateral findings of CTS, no subjective symptoms
- No diabetic polyneuropathy

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Outcome two years later

- Good recovery of muscle strength
- Mild residual weakness of left infraspinatus
- Total paralysis of the right diaphragm
  - Able to walk without shortness of breath on even ground
  - Difficult to lie flat on the back

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Phrenic neuropathy due to neuralgic amyotrophy

Abstract—The authors reviewed the medical records of 33 patients diagnosed with idiopathic phrenic neuropathy and found that 17 patients had clinical features of neuralgic amyotrophy. They concluded that a careful clinical and electrodiagnostic evaluation may implicate neuralgic amyotrophy as a causative disease in patients with apparently isolated phrenic neuropathy.

NEUROLOGY 2006;66:1582–1584

Bryan E. Tsao, MD; Denis A. Ostrovskiy, MD; Asa J. Wilbourn, MD; and Robert W. Shields, Jr., MD

- Prognosis
  - 50% some recovery

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Muscle Nerve 2016 53:337-350

INVITED REVIEW

NEURALGIC AMYOTROPHY: AN UPDATE ON DIAGNOSIS, PATHOPHYSIOLOGY, AND TREATMENT

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Game over

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