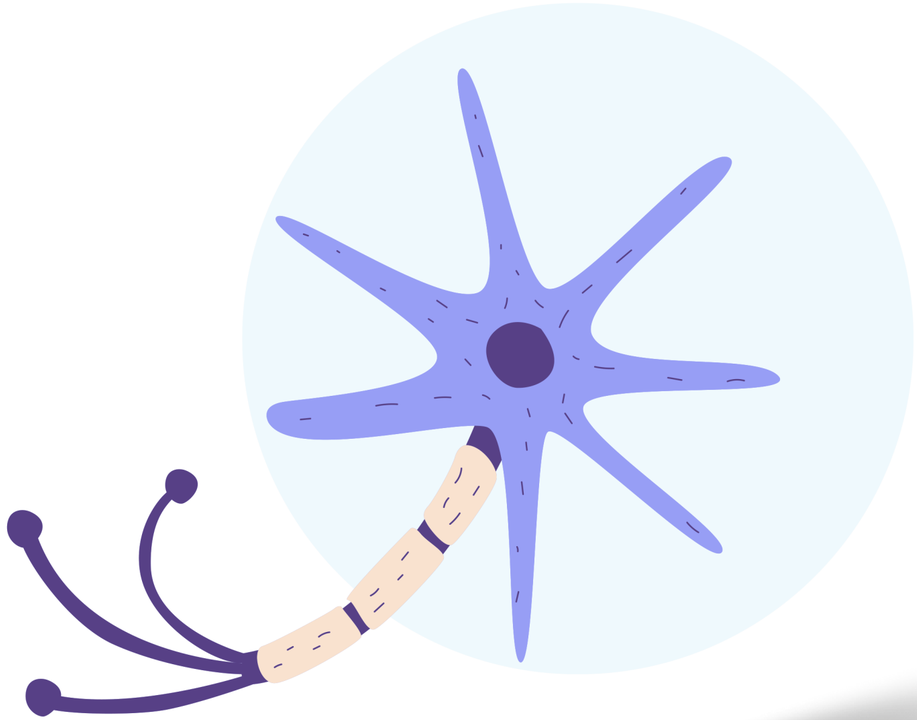
May-2023

Axonal Myeloneuropathy



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Topics to review

Myeloneuropathy

- Definition
- Clinical symptoms
- Disorders
- Conclusion

Definition

Myeloneuropathy: a disorder that affects both the spinal cord and peripheral nerves.

Classification:

- Metabolic: Vitamin B12, B9 deficiency, E deficiency, copper deficiency
- Infectious: HIV, HTLV
- Hereditary disorders: Adrenomyeloneuropathy
- Drugs: Nitrous oxide, Clioquinol
- Paraneoplasic: Breast cancer, Lymphomas
- Inflammatory: Sjögren, Sarcoidosis

Approach to a Case of Myeloneuropathy

1. Clinical recognition of myeloneuropathy
2. Blood levels

Vitamin B12, folic acid, vitamins A, D, E, and K, iron, and calcium

3. MRI of the brain and spinal cord, with contrast
4. EMG and NCS -> axonal sensorimotor polyneuropathy.
5. Identification of myeloneuropathic patterns: clinical, radiographic, and electrodiagnostic
6. Treat the specific cause

CINICAL PATTERNS

SPINAL CORD INVOLVEMENT

- Lhermitte's sign
- Hyperreflexia, Spastic paresis
- Sensory ataxia
- loss vibration and proprioception
- Autonomic dysfunction

PERIPHERAL NERVES INVOLVEMENT

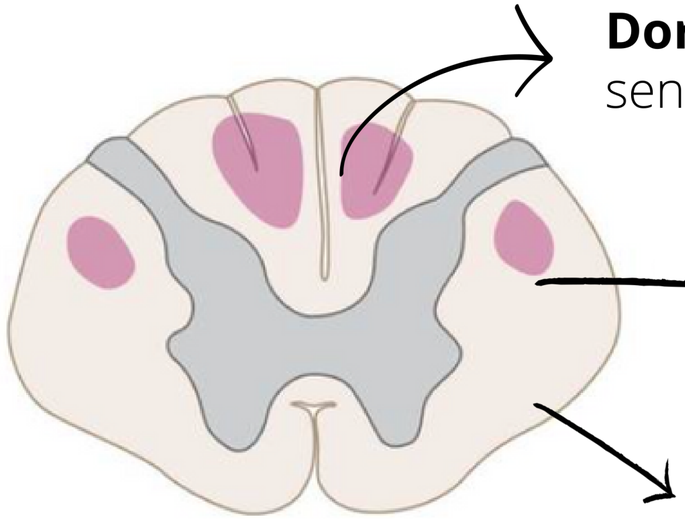
- Distal paresthesia
- Neuropathic pain
- Hyposthesia
- Muscle atrophy

Other etiology-specific symptoms

Causes of Myeloneuropathy

Subacute combined degeneration

- Symmetrical **demyelination** of the spinal cord tracts - insufficient maintenance of myelin



Dorsal column = loss vibration and proprioception, tactile sensation, sensory ataxia (Romberg +)

Lateral columns = Spastic paresis (lateral **corticospinal** tract)

- **Pyramidal signs =** increase deep tendon reflexes, extensor plantar response.

Spinocerebellar tracts and dorsal columns= spinal ataxia

Autonomic dysfuntion = impotence and incontinence , orthostatic hypotension

Neuropsychiatric disease = reversible dementia, depression, paranoia

Causes: Vitamin B12 ↓, Folic acid ↓, Vitamin E ↓, NO intoxication, Copper ↓

Vitamin B12 Deficiency

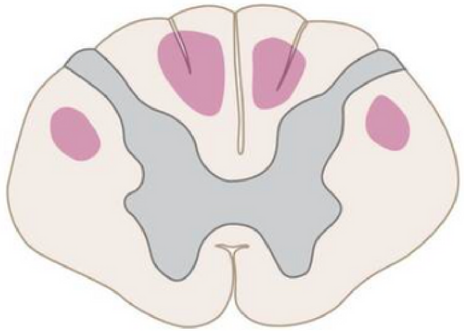
Etiology

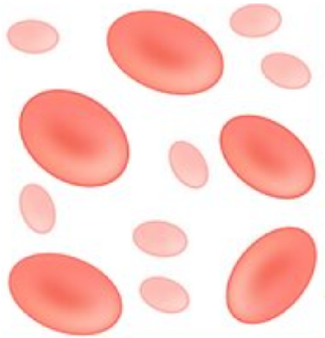
1. **Decrease intake - Malnutrition, restricted diet**
2. **Decrease absorption - Pernicious anemia**
3. **Increase requirement - Pregnancy**

Symptoms

- Subacute combined degeneration of the spinal cord
- Peripheral neuropathy - distal paresthesia (earliest sign), pain, hypoesthesia, muscle atrophy
- Vision loss
- Dementia

Dorsal column: early involvement





Megaloblastic anemia:

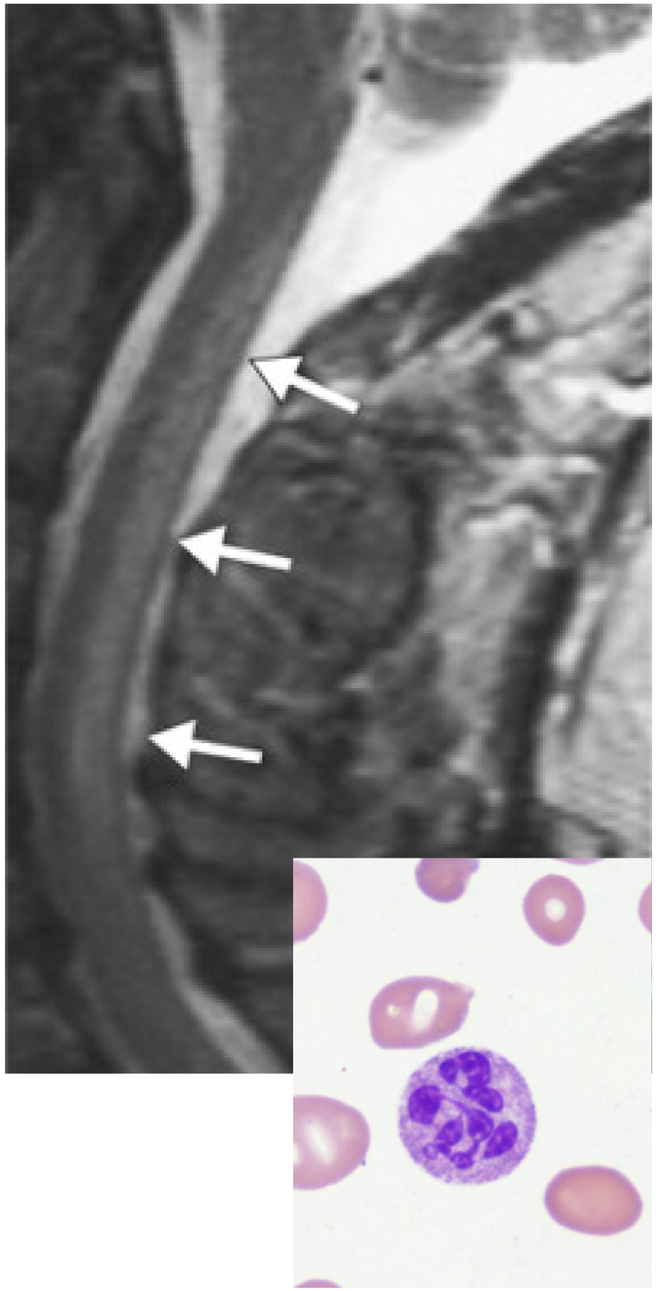
- Glossitis
- Pallor
- Scleral icterus

Findings

- CBC - **megaloblastic anemia** with increased MCV
- Peripheral blood smears - **hypersegmented polymorphonuclear leukocytes**
- **Low serum vitamin B levels** - confirm the diagnosis
- **MRI** T2-weighted signal change in the **posterior** and **lateral columns**, enhance with contrast
- EMG - **axonal peripheral neuropathy**

Tx: Cobalamin 1000 mcg/day IM for 5 days, **monthly** afterward

Neurology **recovery** may be **incomplete**, but **some improvement** over 6-12 months after therapy



Folate deficiency vs Vitamin B12 deficiency

Etiology - less common

- Malabsorption
- Medications = methrotrexate, **phenytoin**, **PPI**, metformin.
- Chronic **alcohol** use

Dx = Elevated homocysteine levels
normal MMA levels

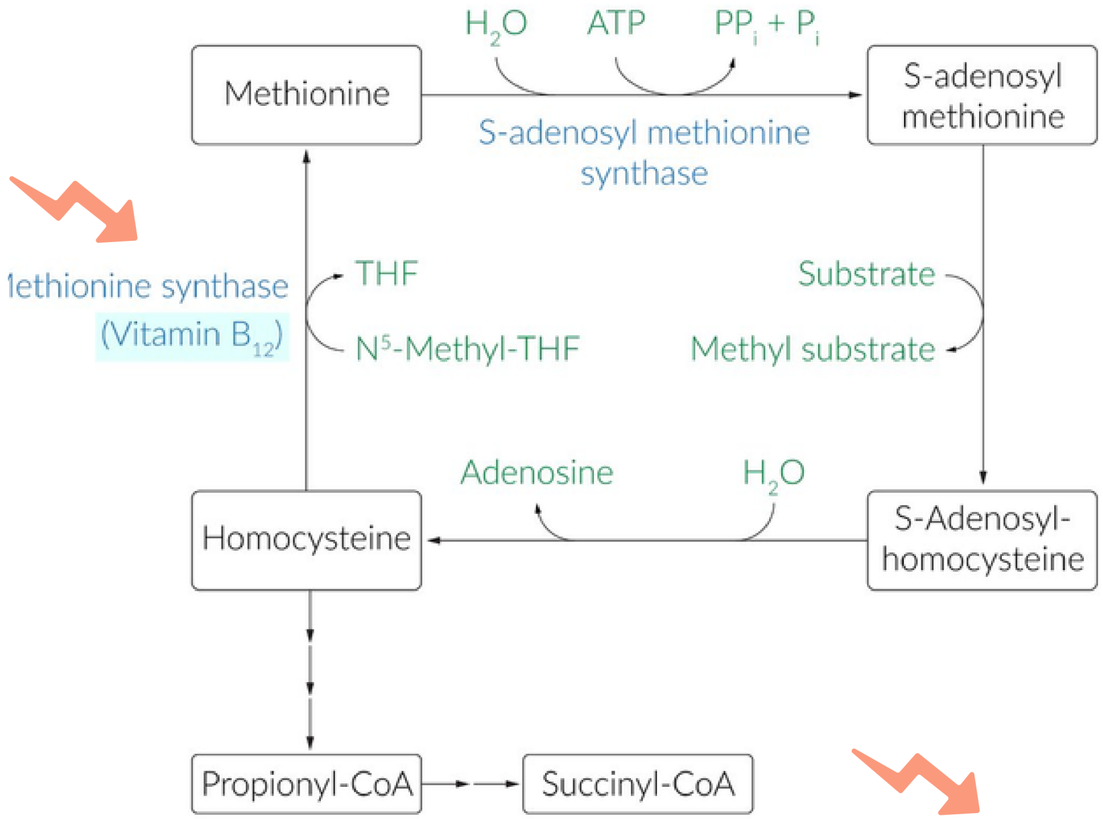
Tx = Folate 1 mg orally 2-3 times per day for several days, followed by 1 mg/day

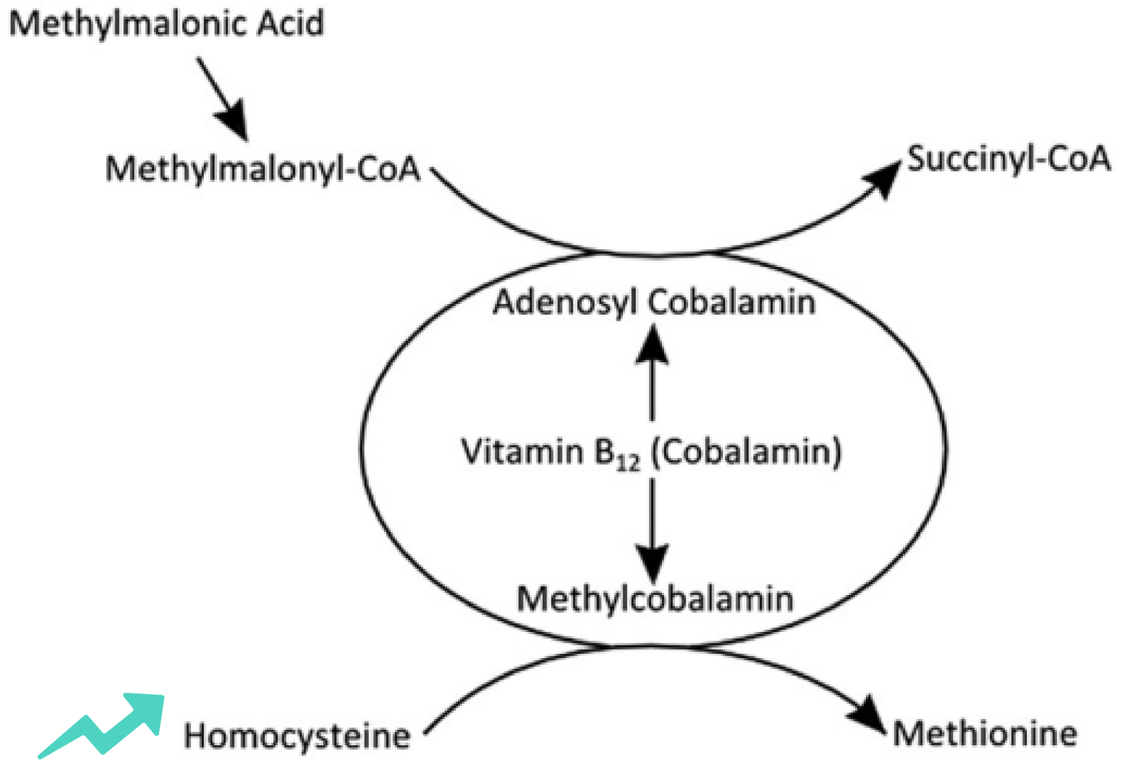
Etiology - prevalence older adults (5-14%)

- Malabsorption
- **Malnutrition**
- Pernicious anemia

Dx= Elevated homocysteine levels
Elevated MMA (methylmalonyl Acid) levels

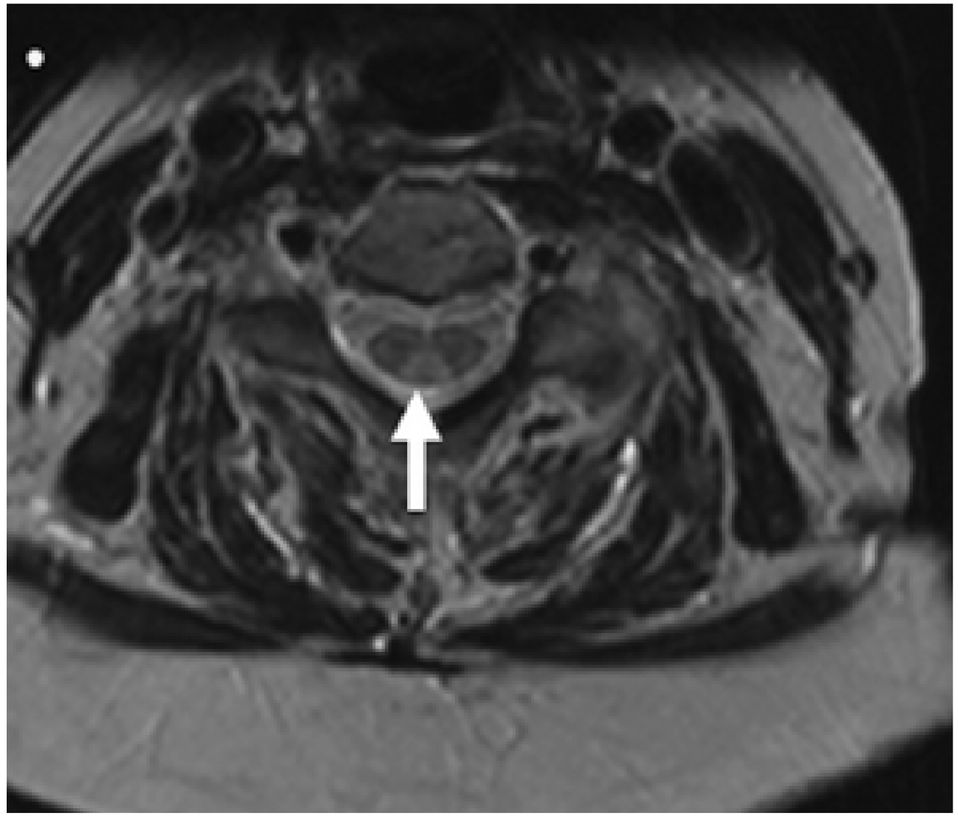
Tx = Cobalamin 1000 mcg/day IM for 5 days, monthly





Demyelination: impaired Fatty Acid Metabolism, decrease methylation process in the myelin, and increase homocystein levels

Copper deficiency



Rare cause, the mechanism is uncertain.
Etiology - Decrease copper absorption

- **Bariatric surgery**
- Malabsorption
- Zinc overload - **OTC product**s

Clinical symptoms:
Myelopathy - Subacute combined degeneration
Peripheral nerve involvement

Dx - low serum copper and ceruloplasmin levels
MRI of the spine - hyperintense lesions in the posterior column

Treatment
Replace copper

- Copper 8 mg/day orally for1 week, 6 mg/day for one week, 4 mg/day for one week, then 2 mg/day
- improvement is variable; **most patients have some residual deficits**

Vitamin E deficiency

Rare cause

Etiology

- **Fat malabsorption disease:** Chronic cholestasis, Pancreatic insufficiency, abetalipoproteinemia,

Clinical

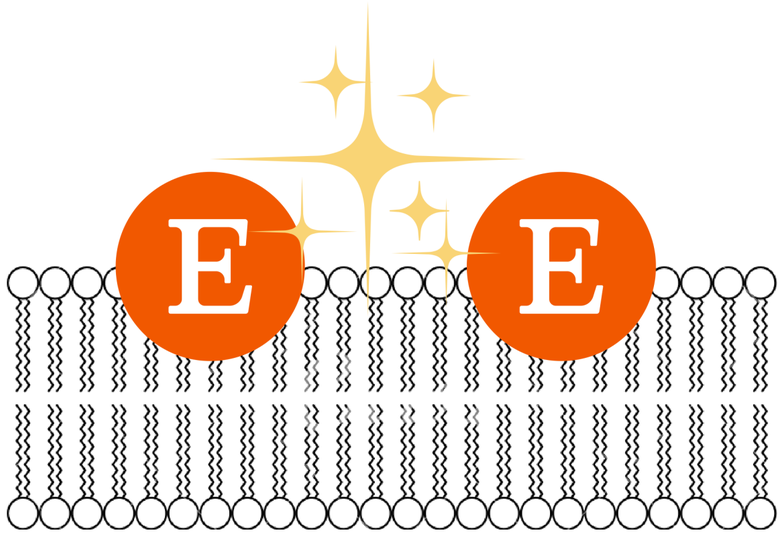
- Ophthalmoplegia
- Retinopathy
- Spinocerebellar syndrome - ataxia
- Myeloneuropathy (dorsal columns) = ataxia, ↓ proprioception and vibration sensation
- Peripheral neuropathy

Dx - Low serum vitamin E levels

EMG - axonal, primarily sensory peripheral neuropathy

Treatment

- Vitamin E 200 IU/day–1000 IU/day



***Vitamin E prevents oxidative damage**

Nitrious Oxide Myeloneuropathy

Importance - NO one of the more commonly used anesthetic agents worldwide.

Recreational NO use - "**whippets**"

Physiopathology - alters colbat core of cobalamin, converting it into an inactive, oxidized form.

time onset: immediately to 2 months following NO exposure

Clinical symptoms:

- Myelopathy
- Peripheral neuropathy
- cognitive changes

Tx: cessation of NO and vitamin B12 IM.

Sensory and motor impairment persisted in most patients.

Paraneoplastic myeloneuropathy

Physiopathology - Immune-mediated response triggered by an underlying malignancy (Breast, Lung, Ovaric, Lymphoma)

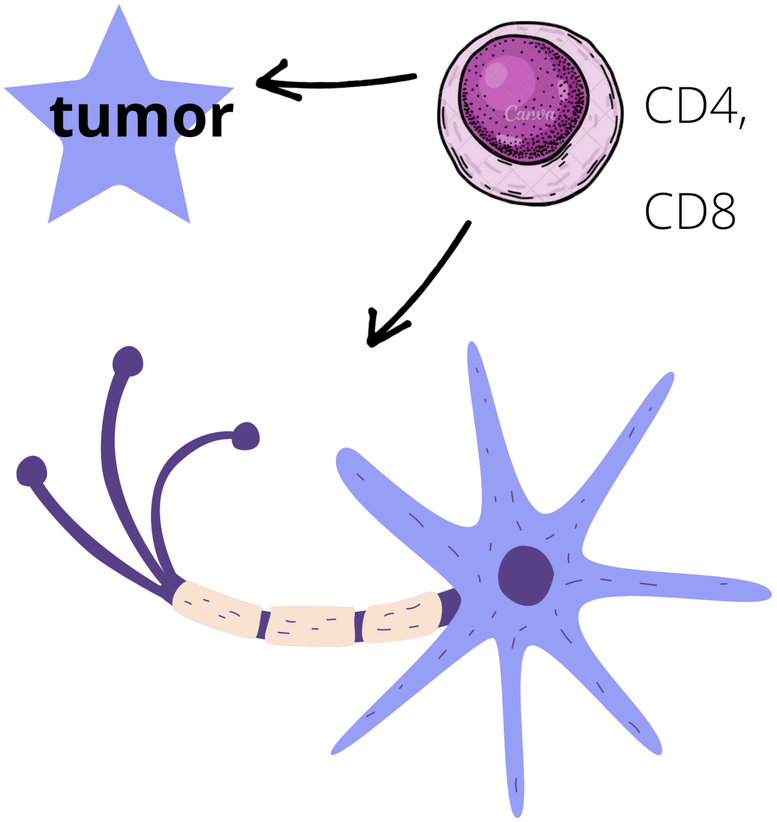
- Molecular Mimicry
- Autoimmune response

Clinical symptoms:

- Myelopathy
- Peripheral neuropathy. - More predominant
- Other: limbic encephalitis, Lambert-Eaton Myasthenic syndrome

Most common association - **Anti-Hu** - present in 2% (of lung cancer)

Treatment: IV methylprednisolone, IV immunoglobulin



Sjögren syndrome

Physiopathology - an autoimmune disorder associated with exocrine gland impairment. Caused by demyelination, myelitis, antineuronal antibodies, antibody-mediated autonomic dysfunction

Clinical symptoms:

- xerophthalmia, xerostomia,
- Myelopathy
- Segmental radiculopathy - often precedes the clinical manifestation

Dx: hyperintensity on T2-weighted cervical spinal cord MRI

Tx: IV methylprednisolone, IV immunoglobulin

methotrexate, cyclophosphamide, azathioprine, chloroquine, infliximab

Myelopathy Associated with Human T-cell Lymphotropic Virus Type I

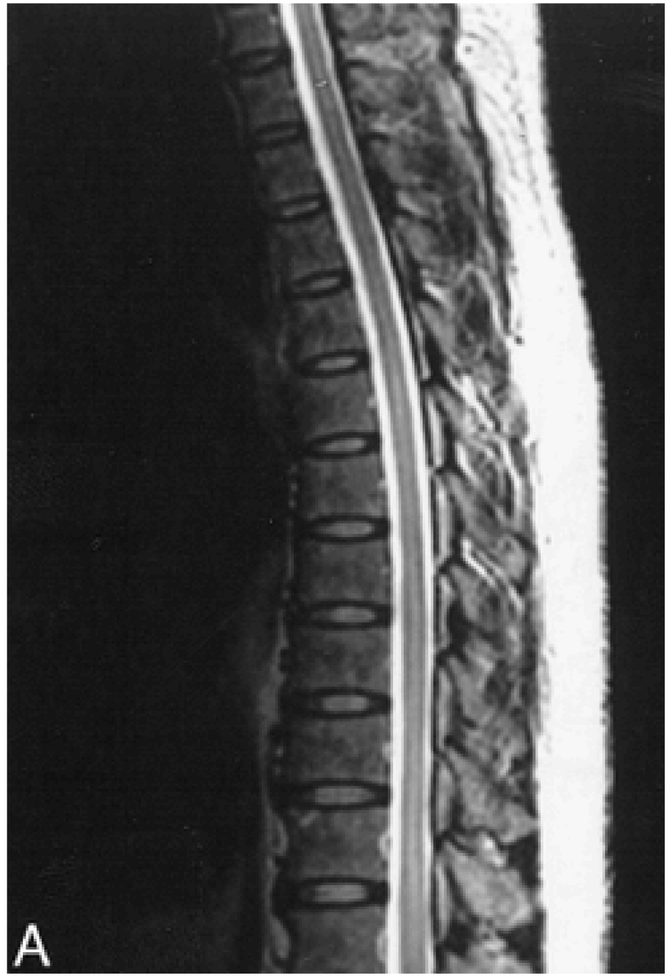
HTLV-1 - retrovirus - transmitted sexually, via contaminated needles, and through breastmilk

HTLV-1 -> immunologic response in the CNS -> neurodegeneration

2% of carries develop - Topical spastic paraparesis

- Progressive myelopathy in equatorial countries
- Spasticity, weakness, hyperreflexia, and urinary symptoms
- Addition: uveitis, alveolitis, polymyositis

Tx: supportive



HTLV-I-Associated Myelopathy: Acute Progression and Atypical MR Findings Miyuki Shakudo, Yuichi Inoue and Tsuyoshi Tsutada American Journal of Neuroradiology September 1999, 20 (8) 1417-1421;

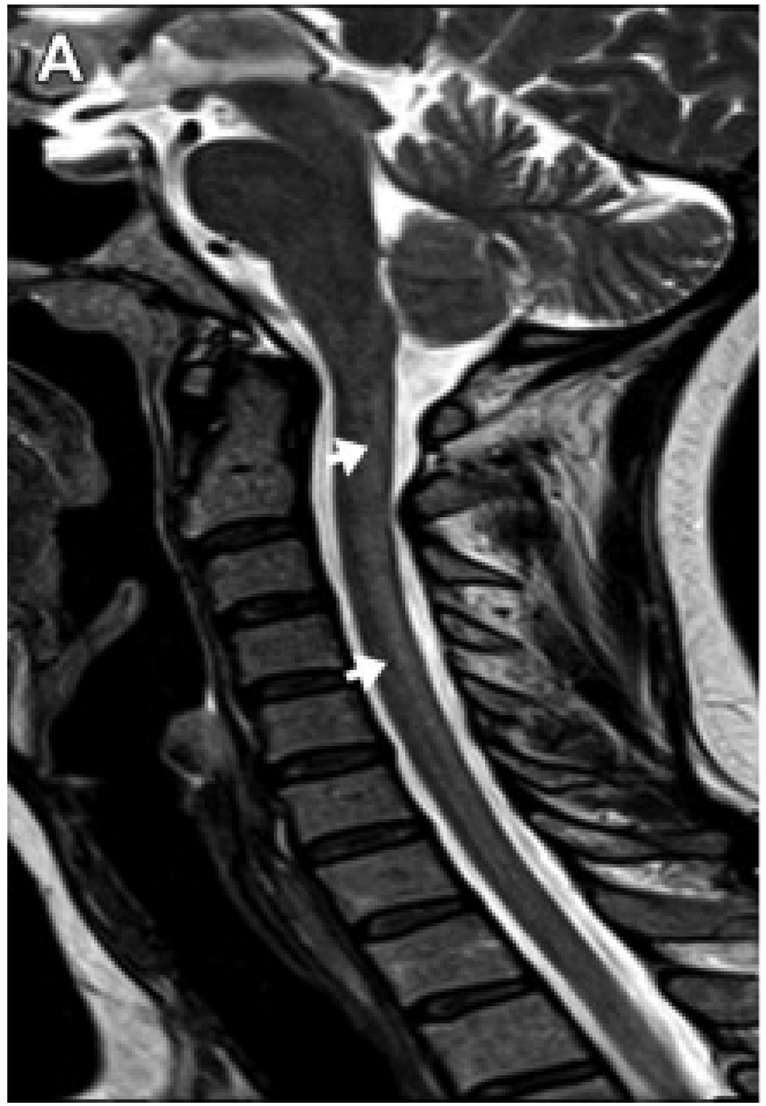
HIV Myeloneuropathy

late stages of HIV infection

Clinical symptoms:

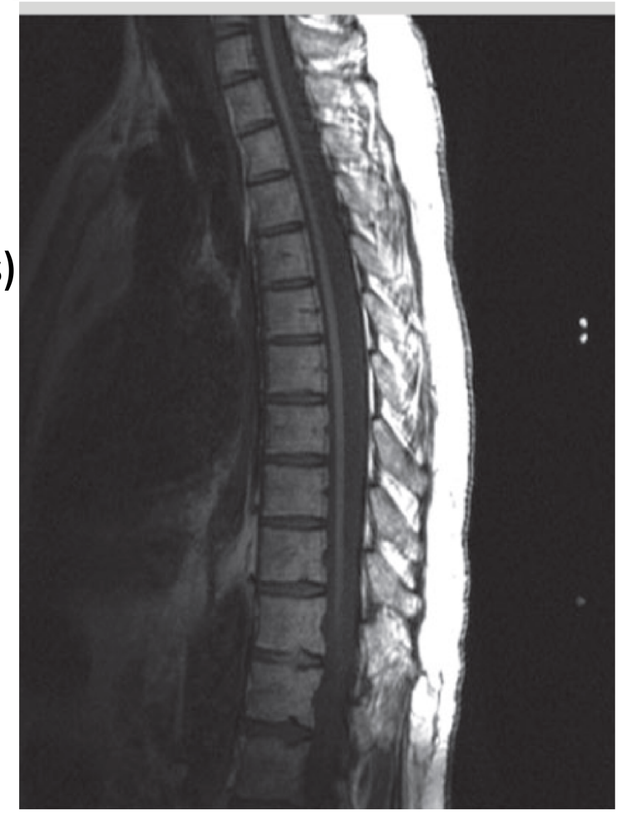
- Vacuolar myelopathy - chronic spastic paraparesis with sensory ataxia and urinary incontinence
- Sensory neuropathy
- AIDS dementia

Tx: highly active antiretroviral therapy (HAART)



Adrenoleukodystrophy - Adrenomyeloneuropathy

slowly progressive spastic paraparesis and myeloneuropathy, X-linked recessive disorder



An X-linked recessive disorder involving the ABCD1 gene.

Adults, mostly men or female carriers, experience

- slowly progressive stiffness and weakness in the legs (spastic paraparesis)
- abnormal sphincter control, neurogenic bladder, sexual dysfunction,
- polyneuropathy (numbness or painful sensations)
- pes cavus (high arches).

Diagnosis: Increase in very long chain fatty acids in plasma.

Treatment: Supportive care.

Prognosis: Most affected males lose the ability to walk unassisted by age 50.

Conclusions

- In conclusion, myeloneuropathy encompasses a group of neurological disorders characterized by the involvement of both the spinal cord (myelopathy) and peripheral nerves (neuropathy). It can present with a wide range of symptoms,
- Early recognition and intervention are essential to prevent or minimize disability

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