Lecture 4

Multiple sclerosis

YouTube

What is Multiple Sclerosis

OBJECTIVE

I. Appreciate the critical role of myelin in maintaining the integrity of the CNS system.

II. Understand the pathogenesis and the clinic-pathological features of multiple sclerosis as the classical and the commonest example of CNS demyelinating diseases.

PRIMARY DISORDERS OF MYELIN

- In general, diseases involving myelin are separated into two broad groups:

Demyelinating diseases of the CNS	Dysmyelinating diseases of the CNS (leukodystrophy)
Acquired conditions	Inherited (Mutated genes)
Characterized by preferential damage to previously normal myelin	Myelin is not formed properly, or has abnormal turnover kinetics
Commonly result from: 1- immune-mediated injury, such as: multiple sclerosis 2- Also viral infection of oligodendrocytes as in progressive multifocal leukoencephalopathy. 3- Drugs and other toxic agents.	Associated with mutations affecting the proteins required for formation of normal myelin or in mutations that affect the synthesis or degradation of myelin lipids

Multiple Sclerosis (MS)

- autoimmune demyelinating disorder .
- The most common demyelinating disorders.
- characterized by distinct episodes of neurologic deficits, separated in time, attributable to white matter lesions that are separated in space.
- It can occur at any age, but it usually begins between the ages of 20 and 50.
- Women are affected twice as often as men, but men has worse prognosis than women.
- The illness shows **relapsing and remitting*** episodes of neurologic deficits
  The frequency of relapses tend to decrease during the course of the illness, but there is a steady neurologic deterioration in a subset of patients.

*Relapsing is episode of attacks of neurologic deficits, while remission is episode of recovery

Pathogenesis

- It is believed to be caused by a combination of environmental and genetic factors that result in a loss of tolerance to self proteins.
- The risk of developing MS is 15-fold higher when the disease is present in a first-degree relative
- The concordance rate for monozygotic twins*(also called identical twins) is approximately 25%, with a much lower rate for dizygotic twins*.
- A significant fraction of the genetic risk for MS is attributable to HLA-DR variants, the DR2 allele being the one that **most significantly increases the risk for developing MS**.
- It caused by T cell-mediated delayed type hypersensitivity reaction (Type IV hypersensitivity) to myelin proteins.
- MS is characterized by the presence of demyelination without the axonal loss, some injury to axons does occur.
- Toxic effects of lymphocytes, macrophages, and their secreted molecules have been implicated in initiating the process of axonal injury, sometimes even leading to neuronal death.

*__monozygotic twins__ originate from a single zygote or fertilized egg , and __dizygotic twins__ come from two zygotes

Morphology

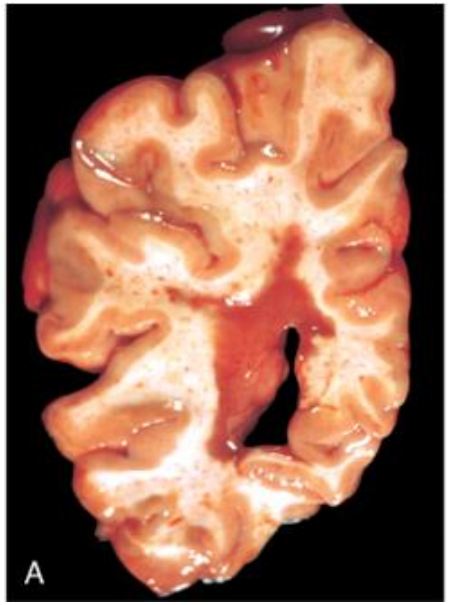
- MS is a white matter disease.

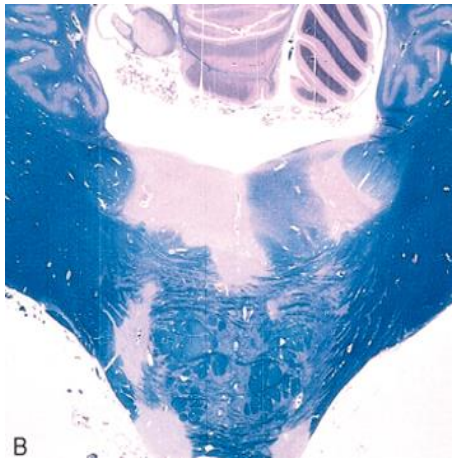
- Affected areas show multiple, well-circumscribed, slightly depressed, glassy, gray-tan, irregularly shaped lesions, termed **plaques**. (Pic A)

- The lesions have sharply defined borders at the microscopic level. (Pic B)

- **ACTIVE PLAQUES:**
  - there is evidence of ongoing استمرار myelin breakdown with abundant macrophages containing myelin debris.
  - Lymphocytes and monocytes are present, mostly as perivascular cuffs.
  - Axons are relatively preserved, although they may be reduced in number.

- **INACTIVE PLAQUES**
  - ❑ No inflammation
  - ❑ No myelin.
  - ❑ Astrocytic proliferation is prominent
  - ❑ Gliosis is prominent.



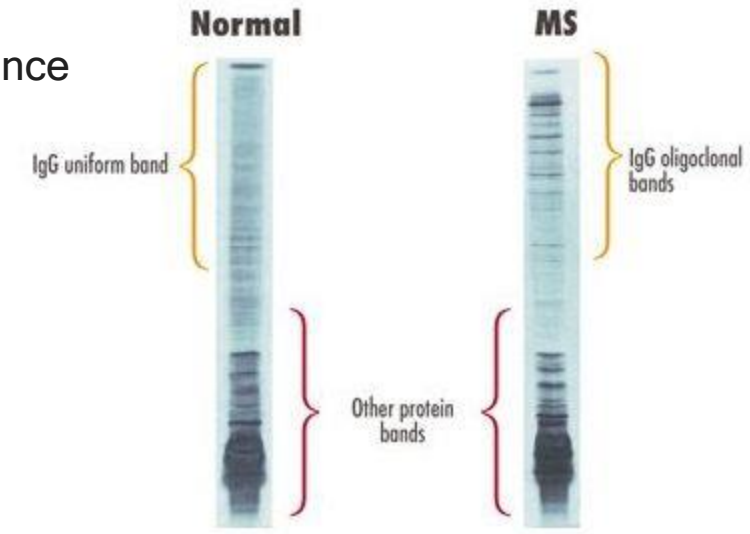


Clinical features

- MS lesions can occur anywhere in the CNS → which may induce a wide range of clinical manifestations.
- visual, motor, and sensory problems being the most common.
- There are more lesions in the brain of MS than that might be expected from clinical examination.
- Multiple relapses followed by remissions, typically, the recovery is not complete, and gradual accumulation of neurologic deficits
- It's hard to predict when the next relapse.

CSF findings

- The marker for MS disease is presence of Oligoclonal Bands* in CSF
- IgG level will increased
- 1/3 of cases there is moderate pleocytosis*



*antibodies directed against a variety of antigenic targets
* an increase in white blood cells (WBCs) count

Summary from Robbins

SUMMARY

Primary Diseases of Myelin

- Because of the critical role of myelin in nerve conduction, diseases of myelin can lead to widespread and severe neurologic deficits.
- Diseases of myelin can be grouped into *demyelinating diseases* (in which normal myelin is broken down for inappropriate reasons—often by inflammatory processes), and *dysmyelinating diseases* (metabolic disorders that include the leukodystrophies in which myelin structure or its turnover is abnormal).
- Multiple sclerosis, an autoimmune demyelinating disease, is the most common disorder of myelin, affecting young adults. It often pursues a relapsing-remitting course, with eventual progressive accumulation of neurologic deficits.
- Other, less common forms of immune-mediated demyelination often follow infections and are more acute illnesses.

CHALLENGE YOUR SELF

1- MS is strong associated with

A. HLA-A
B. HLA-DQ
C. HLA-DR2
D. HLA-DP

2- The concordance rate for monozygotic twins to have MS are

A. 25%
B. 70 %
C. 100 %
D. 50%

3- Symptoms of multiple sclerosis include

A. Numbness
B. Difficulty with walking
C. Problems with urination
D. All of the above

4- Multiple Sclerosis usually affects

A. Children
B. Young adults
C. Older age group

5- in inactivated plaque there is evidence of ongoing myelin breakdown

A. T
B. F

1- C
2- A
3- D
4- B
5- B

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