AMYLOIDOSIS

Q) definition, gross & microscopy of organs involved in 2° amyloidosis.
special stains - table in Rama - page 184, 185.
pathogenesis?
physical & chemical nature.
spleen
Q) 1° & 2° type & other type Q) CF?
Q) classification - table. Q) diagnosis?
Q) mc & gram in 1°?

definition.

It is a condition associated with a number of inherited and inflammatory disorders in which extracellular deposits of fibrillar proteins are responsible for tissue damage and functional compromise.

Physical Nature

seen through.

- Electron mc
  - continuous, ✓
  - non branching ✓
  - fibrils ✓
  - 7.5 - 10nm diameter
- X-ray crystallography and Infrared spectroscopy
  - characteristic cross linked β-pleated sheet conformation.
  - responsible for distinctive congo-red birefringence of amyloid.

Chemical Nature

95% - fibril protein
5% - Glycoproteins & 'P' component.

Biochemical forms

major forms (3). minor forms (>2)

AL AA Aβ ATTR $A\beta_2M$ AApoA

amyloid light chain - AL-amyloid.

consists of.

① complete Ig light chains
② amino-terminal fragments of light chain
③ or both.

m/c → made of λ Light chains.

- seen in plasma cell tx.
- monoclonal B cell proliferation.
- they are produced by plasm cells.

{monoclonal ⇒ same type light chain in abundance}

Amyloid Associated type.

AA-amyloid. - made from SAA protein ("Serum associated & amyloid." associated. protein.

inflammation.
↓
IL-6, IL-1.
↓
↑ synthesis of SAA from liver.

- associated with chronic inflammation.
→ called as 2° amyloidosis.

β-Amyloid protein — A-β type.

: derived from a transmembrane glycoprotein called
↓
Amyloid precursor protein

→ forms core of cerebral plaques in alzheimer's disease.

Minor types:

① Transthyretin — TTR.

Normal serum protein that,
↓
transports – thyroxine & retinol

- mutations in gene coding TTR → structure alteration → misfolding

Seen in
- familial amyloid polyneuropathy
- heart of aged people – senile systemic amyloidosis.

β_2 microglobulin

- normal serum protein.
- Aβ_2 m is formed from β_2 microglobulin.
↓ seen.
PT's on long term hemodialysis.

pathogenesis

flow chart in textbook page – 182. also in Robbins not.

Morphology of Organs Involved.

main organs involved in:

1° amyloidosis → Heart, GIT, resp tract, peripheral N, skin, tongue.

2° amyloidosis → kidney
spleen
lymph node.
liver
adrenals
thyroid.

Morphology

KIDNEY

- m/c and serious form of organ involvement.

GROSS

Initially → normal size & colour.

In advanced stages → shrunken due to vascular narrowing induced by deposition of amyloid within arterial & arteriolar walls.

Microscopy

- mc AL, AA type.

main site of deposition : Glomeruli

Glomerular deposits
↓
1st causes thickening of mesangeal matrix
↓
followed by widening of BM of glomerular capillaries.
↓
capillary lumen narrowing + glomerular architecture ruined → shows broad ribbons of amyloid.

• ~~deposits are also seen in peritubulo~~.

SPLEEN

GROSS

• moderate - marked Splenomegaly

2 patterns

SAGO Spleen.

↓

localyed amyloid deposits involving {limited} to splenic follicles.

↓

GROSSLY appears like tapioca/ sago granule

↓

SAGO spleen.

Lardaceous spleen

↓

amyloid involves walls of splenic sinuses & CN-tissue framework in redpulp

↓

fusion of early deposits give rise to large mass like areas of amyloidosis

↓

resemble pig fat {lardaceous}

↓

lardaceous spleen.

Light MC

• amyloid - pink colour. homogenous.

LIVER

GROSS

• moderate - marked hepatomegaly.

• advanced st

→ pale, grey, waxy.

MC

amyloid 1st deposits in

↓

space of Disse

↓

thin encroaches on adjacent Hepatocytes & Sinusoids.

↓

deformity & pressure atrophy of hepatocytes

↓

replacement of large portions of liver parenchyma.

but LFT normal..

HEART

• involved in 1° {systemic amyloidosis.

• major organ involved in senile systemic amyloidosis

GROSS

• can be enlarged & firm.