AMYLOIDOSIS

Types, Diagnosis & Treatment

Introduction

- Group of heterogenous disorders
- Extracellular deposition of insoluble fibrillar protein **called Amyloid**, resistant to degradation
- Structural and functional organ dysfunction
- Acquired or Hereditary
- Localized or Systemic

Types

According to Distribution

1. Localized
   - Brain - Alzheimer's disease
   - Joints and Carpal Tunnel - Hemodialyzed patients
2. Systemic

Types

1. Primary Amyloidosis (AL)
2. Secondary Amyloidosis (AA)
3. Hereditary Amyloidosis
4. Hemodialysis-related Amyloidosis
5. Senile Amylodosis

Primary Amyloidosis (A**L**)

- Fibril protein precursor - Monoclonal Immunoglobulin **L**ight chains
- Overproduction of light chains - Monoclonal gammopathies like myeloma, Waldenstrom macroglobulinemia, plasmacytomas
- *Kappa* and *lambda* light chains
- Symptoms depends on organs involved

Primary Amyloidosis (A**L**)

- **Heart** - Cardiac failure
- **Renal** – Proteinuria, nephrotic syndrome
- **Nervous** - Carpal tunnel syndrome, peripheral and autonomic neuropathy
- **GI-involvement** - Malabsorption, Weight loss, Hemorrhage, Perforation, Obstruction, Hepatomegaly and Macroglossia
- **Vessels** - Spontaneous purpura *especially* characteristic periorbital

Treatment

Chemotherapy as myeloma, autologous stem cell transplant

Secondary Amyloidosis (A**A**)

- Fibril protein precursor - Protein A – an acute phase reactant - a precursor of serum amyloid **A**
- Secondary to Chronic infections and inflammation
  - TB, Bronchiectasis, RA, ulcerative colitis/Crohn's disease, osteomyelitis
- Affects kidneys, liver and spleen
- Presents with proteinuria, nephrotic syndrome, and hepatosplenomegaly
- *Macroglossia is not seen and cardiac involvement is rare*

Treatment

Optimal management of the underlying condition

Familial or hereditary Amyloidosis (ATTR)

- Autosomal dominant
- Abnormal transthyretin (ATTR) – *a plasma carrier protein* – due to mutations
- Produced by **Liver**
- Presents with
  - Peripheral or autonomic neuropathy
  - Cardiomyopathy
  - *Renal involvement unusual*

Treatment

Liver transplant can be curative

Dialysis-associated ($A\beta_2M$) Amyloidosis

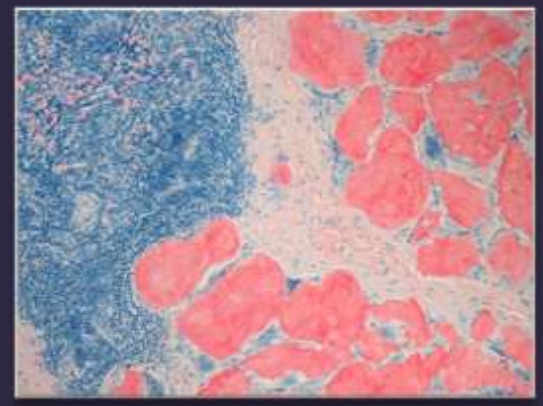
- Accumulation of circulating β_2-macroglobulin in patients on dialysis
- Poorly filtered by dialysis membrane
- Manifestation occurs 5 – 10 years after the start of dialysis
- Clinical Features
  - Carpal tunnel syndrome
  - Chronic arthropathy and pathological fractures secondary to amyloid bone cyst

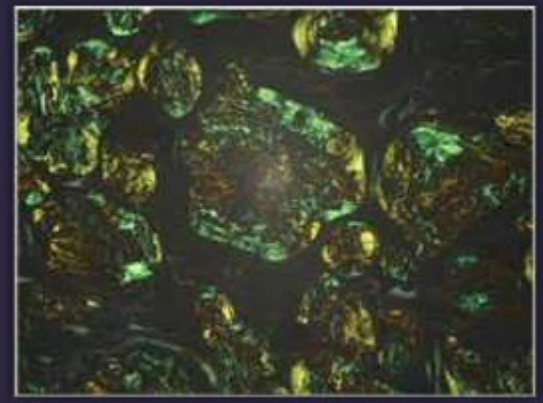
Senile systemic amyloidosis

- Feature of normal ageing
- Normal transthyretin protein deposited in tissues
- Age > 70 years
- Affects > 90% of 90-year-olds
- Usually asymptomatic

Diagnosis

- **Biopsy and Congo Red staining**
  - Abdominal fat or rectal biopsy – noninvasive with 80% yield
  - Organ biopsy
  - Amyloid deposits stain **Red**
  - Show Apple-green fluorescence in polarized light
  - *Immunohistochemical staining* - Identify type of amyloid fibril
- **Quantitative scintigraphy**
  - ^{123}I-labelled serum amyloid P
  - A valuable tool in determining the overall load and distribution of amyloid deposits





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