PATHOLOGY

MD 3

PATHOLOGY

AMYLOIDOSIS

Amyloidosis

Learning Objectives

- Answer questions about composition of amyloid
- Explain information related to systemic types of amyloid
- Demonstrate understanding of localized types of amyloid

Amyloidosis

COMPOSITION OF AMYLOID
Amyloidosis is a group of diseases characterized by the deposition of an extracellular protein that has specific properties.

- Individual molecular subunits form β-pleated sheets. Amorphous eosinophilic extracellular deposits of amyloid are seen on the H&E stain. These deposits stain red with the Congo red stain, and apple green birefringence
  of the amyloid is seen on the Congo red stain under polarized light.
- The fibrillary protein of amyloid varies with each disease. Also present in amyloid are serum amyloid P (SAP) and glycosaminoglycans (heparan sulphate).

Amyloidosis

SYSTEMIC TYPES OF AMYLOID

- Primary amyloidosis has amyloid light chain (AL) amyloid, whose fibrillary protein is made of kappa or lambda light chains. Primary amyloidosis may be seen in plasma cell disorders (multiple myeloma, B-cell lymphomas, etc.) but most cases occur independent of other diseases.
- Reactive systemic amyloidosis (secondary amyloidosis) has amyloid-associated (AA) protein, whose precursor is serum amyloid A (SAA), an acute phase reactant produced by the liver which is elevated with ongoing chronic inflammation and neoplasia. Reactive systemic amyloidosis can be seen with a wide variety of chronic diseases, including rheumatoid arthritis, systemic lupus erythematosus, tuberculosis, bronchiectasis, osteomyelitis, inflammatory bowel disease, and cancer.

Amyloidosis

- Familial Mediterranean fever has AA type amyloid with fibrillary protein composed of serum amyloid A (SAA). This autosomal recessive disease is characterized by recurrent inflammation, fever, and neutrophil dysfunction. Gain of function mutations of pyrin are present.
- Hemodialysis-associated amyloidosis has Aβ2M type amyloid with precursor protein β2-microglobulin. This form of amyloidosis may cause carpal tunnel syndrome and joint disease.

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LOCALIZED TYPES OF AMYLOID

- Senile cerebral amyloidosis (Alzheimer disease) has Aβ type amyloid with fibrillary protein composed of β-amyloid precursor protein (βAPP). It is found in Alzheimer plaques and in cerebral vessels. The gene for βAPP is located on chromosome 21.
- Senile cardiac/systemic amyloidosis has ATTR type amyloid with fibrillary protein composed of transthyretin. This type of amyloidosis is seen in men older than 70 years and may cause heart failure as a result of restrictive/infiltrative cardiomyopathy. Four percent of African Americans have a transthyretin (TTR) V1221 mutation with 1% being homozygous, serving as a risk for cardiac disease.
- Endocrine type amyloidosis is seen in medullary carcinoma of the thyroid (procalcitonin), adult-onset diabetes (amylin), and pancreatic islet cell tumors (amylin).

Amyloidosis

CLINICAL FEATURES

In systemic forms of amyloidosis, the kidney is the most involved organ, and patients may experience nephrotic syndrome and/or progressive renal failure. Cardiac involvement may cause restrictive cardiomyopathy and conduction disturbances. Other clinical features include hepatosplenomegaly and involvement of the gastrointestinal tract, which may produce tongue enlargement (macroglossia, primarily in AL type) and malabsorption. Diagnosis in systemic forms of amyloidosis can be established with biopsy of the rectal mucosa, gingiva, or the abdominal fat pad; Congo red stain shows apple green birefringence under polarized light of amyloid deposits. The prognosis of systemic amyloidosis is poor. AL amyloidosis is diagnosed by serum and urinary protein electrophoresis and immunoelectrophoretic. Proteomic analysis is another diagnostic tool.

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