Amyloidosis
Overview

• Plasma proteins polymerize forming fibrils of anti-parallel $\beta$-pleated sheet that are deposited in tissues

• Clinical manifestations, treatment, and prognosis depend upon type of protein involved
Epidemiology

- Prevalence ~1/100,000
- Incidence in U.S. ~2,500
- Median age at diagnosis is 64
- Only 1% are < 40 years old
- 78% primary (AL), 6% familial, 2% secondary (AA)
Major Types

- **AL** -- Immunoglobulin Light chains
- **AA** -- Acute phase reactant SAA
- Dialysis-related -- $\beta$-2 microglobulin
- Heritable -- e.g. Transthyretin
- Organ Specific -- e.g. APP in Alzheimers
AL (Primary)

- Occurs by itself, or . . .
- Can be associated with multiple myeloma or Waldenstrom’s
- 75% $\lambda$ light chains--variable region
- Monoclonal plasma cells in marrow
AL (Primary)-Presentation

- Weakness, fatigue, weight loss
- Nephrotic syndrome +/- renal failure
- Congestive cardiomyopathy (e.g. CHF)
- Peripheral neuropathy (e.g. CTS)
- Hepatomegaly
AL (Primary)-Presentation
GI Amyloidosis

- Mucosa of duodenum (100%), stomach & colorectum (90%), esophagus (70%)

- Neuromuscular infiltration

- Causes nausea, vomiting, bleeding, gastroparesis, constipation, dysphagia, pseudo-obstruction, malabsorption, bacterial overgrowth, protein losing enteropathy.
Hepatic Amyloidosis

• 70% of AL

• Median survival = 9 months

• Elevated ALP (86%), weight loss (72%), fatigue, pain, anorexia, HSM, ascites, edema
AL (Primary)-Diagnosis

- **Suspicious** = clinical findings + proteinuria & paraprotein in 85-90%

- **Definitive Dx** = biopsy of involved organ (abdominal fat pad, rectum, kidney, liver, skin)
AL (Primary)-Prognosis

• Death from CHF (51%), hepatic failure, infection

• 0.4% delayed progression to myeloma

• Worse prognosis if plasma cells >0.5/µL, β2 microglobulin >2.7, marrow plasma cells >10%, cardiac involvement

• 50%, 15%, 5% survival at 1, 5, 10 years
AL (Primary)-Treatment

• Supportive = Cardiac (diuretics), renal (dialysis), GI (pro- & anti-motility agents, anti-emetics, antbx for bacterial overgrowth, nutritional support)

• Melphalan & prednisone doubled survival compared to colchicine (8 vs. 16 months)

• High-dose chemo with peripheral stem cell rescue (experimental)
AA (Secondary)

- Associated with chronic inflammation (RA, IBD, osteomyelitis) causing polymerization of serum amyloid A protein
- Renal insufficiency more common
- Rarely involves heart or nerves
- Median survival 2 yrs
- Treat underlying disease
Questions?