Familial Amyloidosis from the Pathologist’s perspective

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Outline:

1. How amyloid is diagnosed
2. Congo red stain and issues with diagnosis of amyloid
3. Types of biopsies
4. Issues specific to familial amyloidoses
Routine stain in pathology:
Hematoxylin (blue) and eosin (pink)
Suspecting amyloid: ★ point to relatively large areas with homogeneous deposits devoid of cells. Such areas are suspicious for amyloid. Since other pathologies can look similar, Congo red stain is needed to verify the suspicion of amyloid. Caveat: small deposits may not be apparent on a routine stain!
Congo red = bright red color:
- first synthesized in 1883 by Paul Bottiger as a textile dye
- subsequently marketed under the name "Congo red"
since at that time Africa and things associated with it were very fashionable
- Since early 1920s used in pathology to stain amyloid
Amyloidoses

Normal proteins: α helix

Amyloid: β pleated sheet

Amyloid formation = conformational shift to β-pleated sheet structure

Why amyloid forms?
- structural abnormalities due to a genetic defect (familial)
- excess production…(see other presentations)
Congo red binding sites
All types of amyloid have β-pleated sheet conformation
All types stain with Congo red
All types are fibrillar under a very high magnification (electron microscope)
First step: Congo red stain viewed in regular light, deposits of amyloid stain red
Need a second step, i.e. to demonstrate apple green birefringence under polarized light (need a polarizer attached to a regular microscope, small deposits difficult to see...
Current gold standard

Diagnostic result = apple green birefringence (deposits are green like a green apple in the insert)
This picture shows a kidney biopsy with amyloid in the glomerulus seen in the center
**Diagnosis of amyloid –**

**When** to do Congo red stain?
- to confirm suspicion of amyloid
  (usually larger deposits suspected on a routine stain)
- to **rule out** amyloid
  (in early stages when amyloid deposits are small and not apparent on a routine stain)

**Kidney biopsy:** patients with protein in urine (proteinuria), rarely kidney failure
Since kidney biopsies are routinely examined with additional stains and techniques, amyloid is more often detected than in other tissues

**Heart (native) biopsy:** routinely, heart failure, orthostatic hypotension

**Nerve biopsy:** routinely

**Gastrointestinal biopsies:** many mimickers, many biopsies in daily work, decision which cases should be stained with Congo red is more difficult

**Other specimens – similar to above**
Also enlarged liver, other glands. In general - unexplained kidney, heart or systemic disease should be suspicious for amyloidosis
Fat biopsy – amyloid deposits are irregularly distributed
Larger specimen is better
Small surgical fat biopsy is better than biopsy done via a syringe
Detection of early deposits which are small is most challenging
Second opinion if initial pathology reported as negative
Pathology of Familial amyloidoses:

1. Detection of amyloid in the index (first in the family) patient
   - lack of a family history
   - new mutation
2. Examination of family members/known carriers
   - experience from domino liver transplants
3. Staging, definition of organ involvement
4. Education, increased awareness …