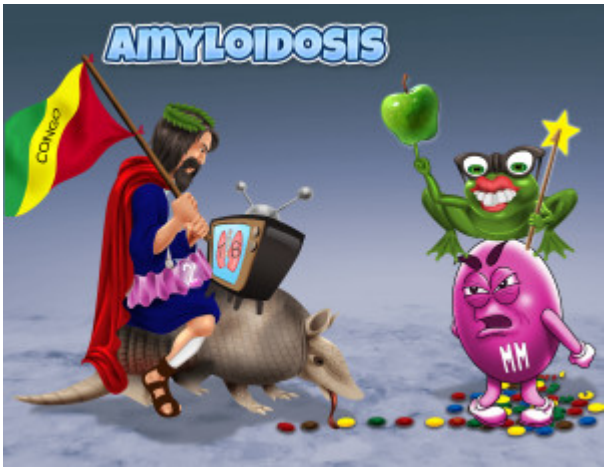
Amyloidosis

Amyloid is a pathologic proteinaceous substance caused by abnormal folding of proteins that can deposit in the extracellular space in various tissues and organs. There are several distinct forms of amyloid proteins and the most common forms include AL (amyloid light chain) derived from Ig light chains from plasma cells and AA (amyloid associated) derived from a non Ig protein from the liver. There is also an AB form associated with beta amyloid precursor protein found in the cerebral lesions of Alzheimer disease. On light microscopy and H&E stains, amyloid appears as eosinophilic, hyaline extracellular substance that can encroach on and produce pressure atrophy of adjacent tissue. To differentiate amyloid from other hyaline deposits like collagen and fibrin, a Congo red stain is commonly used which produces an apple green birefringence when viewed under polarized light. The AL form derived from Ig light chains is commonly called primary amyloidosis and is associated with multiple myeloma. The second major class is associated with chronic inflammatory states as the production of AA protein is part of the acute phase response. This type is often called secondary amyloidosis and is related to chronic diseases like tuberculosis and rheumatoid arthritis. The kidney is the most common organ involved and can manifest as nephrotic syndrome.



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Etiologies

Primary

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Multiple Myeloma

MM character

Multiple myeloma (MM) is a malignancy of plasma cells. Normal plasma cells produce immunoglobulins, which are proteins composed of two heavy chains and two light chains. In MM, the abnormal cells produce only light chains instead. These light chains build up in various tissues and cause the disease known as AL amyloidosis

Secondary

(2) Tutu

In any inflammatory state, the body releases proteins called acute phase reactants. One of these is named serum amyloid A (AA), a small protein produced by the liver. In chronic inflammatory states like rheumatologic diseases or chronic infection, huge amounts of amyloid A are produced, and are deposited in various tissues. This causes the disease known as secondary AA amyloidosis

Tuberculosis (TB)

TB-TV

Because tuberculosis is often a chronic infection, it induces a chronic inflammatory state. This causes the liver to overproduce amyloid A, leading to secondary AA amyloidosis.

Rheumatoid Arthritis

Roman King-Arthur

Because rheumatoid arthritis is a chronic inflammatory state, this causes the liver to overproduce amyloid A, leading to secondary AA amyloidosis.

Pathology

Congo Red Stain

Congo-flag

On light microscopy and H and E stains, amyloid appears as eosinophilic, hyaline, extracellular substance that can encroach on and produce pressure atrophy of adjacent tissue. To differentiate amyloid from other hyaline deposits like collagen and fibrin, a Congo red stain is commonly used which produce an apple green birefringence when viewed under polarized light.

Apple Green Birefringence

Green-apple

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Complications

Nephrotic Syndrome

Nerd-frog

Nephrotic syndrome is the combination of heavy proteinuria (3.5g/day) with other clinical findings such as generalized edema, hypoalbuminemia, and hyperlipidemia. It has many etiologies, one of which is amyloidosis. When amyloid proteins are deposited in the kidneys, they prevent normal glomerular function and result in proteinuria and therefore nephrotic syndrome.