

Multiple Myeloma (MM) (Monday, October 22, 2001)

- B lymphoid malignancy characterized by the proliferation of malignant plasma cells
- MM behaves as a solid tumor with a particular liking to disseminate in metastatic clusters in the marrow cavity.
- MM originates in lymph nodes, first appear in the BM, and seldom in blood.
- MM is a disease of the elderly; incidence in African-Americans is 2x of Caucasian.
- The net result of MM is a devastating and dispiriting syndrome:
- MM was first described in 1844 by Solly and was called "molitites ossium"; and then in 1845 by MacIntyre in London.

Pathophysiology of Multiple Myeloma (MM)

- Many problems associated with MM include:
 - plasma cell tumor that secrete substances;
 - synthesis of large quantities of monoclonal antibodies.
- Most common presenting features in MM are:
 - bone pain;
 - hypercalcemia;
 - osteolysis;
 - uremia;
 - anemia;
 - respiratory tract infections secondary to defective humoral immunity.

Pathophysiology of Multiple Myeloma (MM), continued

Skeletal Abnormalities

- Osteolytic lesions with a characteristic "punched-out" look
- Bones affected include the ribs, sternum, pelvis and vertebrae.
- As the disease progresses, involvement of the skull and proximal ends of the long bones occurs:
- Pathological collapse of the lumbar or dorsal vertebrae with acute lower back pain is a classic form of presentation.
- Osteolysis leads to hypercalcemia



Renal Failure

- ~50% have significant renal impairment at presentation, but many more enter renal failure during the course of the disease.
- Ig light chains secreted by the malignant plasma cell
- Precipitation and deposition of these light chains called "casts".
- Casts can rupture in the kidney and can result in extensive fibrosis and renal failure.
- "Myeloma kidney"

•Threat of renal failure mandates vigilant attention, because kidney failure is going to happen.

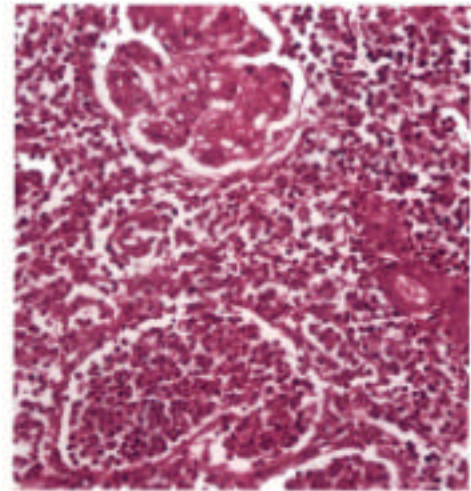
•If renal failure is irreversible, maintenance hemodialysis is used.

Amyloidosis

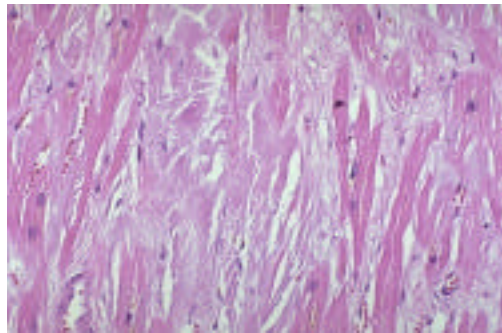
•Amyloid deposits consist of partially degraded immunoglobulin light chains arranged in a rigid, pleated fibrillar structure

•15% of MM cases, amyloid deposits accumulate and inflict damage to kidney, liver, spleen, heart, GI tract, and tongue.

•>70% of these cases will have significantly heart enlargement

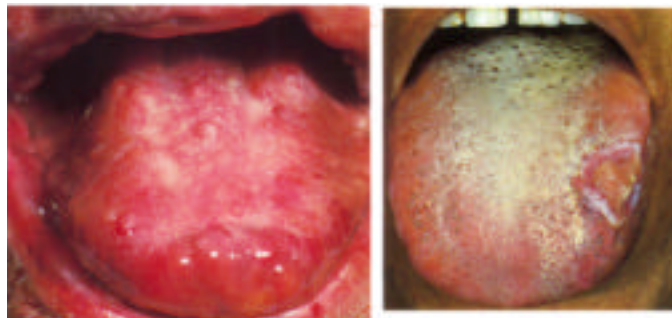


Multiple myeloma: destruction of the renal parenchyma and acute inflammatory cellular infiltration of the interstitial tissues and tubular spaces in pyelonephritis.



Amyloidosis is characterized by deposition of increasing amounts of an amorphous proteinaceous material in one or more tissues.

•A particular distressing manifestation of amyloid deposits is macroglossia, extreme swelling and hardening of the tongue.

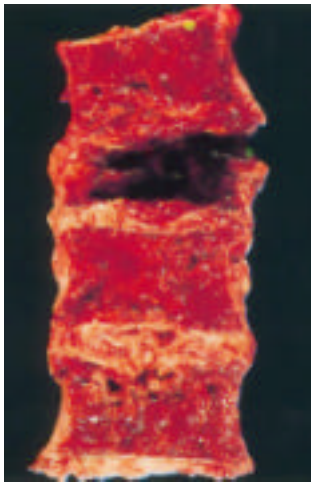


Macroglossia in MM.

Pathophysiology of Multiple Myeloma (MM), continued

Neurological Complications

- The major neurological complications of MM are:
 - nerve tissue compression;
 - mental confusion and other CNS symptoms;
 - peripheral neuropathy, and carpal tunnel syndrome
- Most serious complication is spinal cord compression by localized tumor deposits in the vertebrae, manifest as:
- These changes are usually irreversible. To attempt to treat these patients, it is vital to perform decompression surgery, and to perform radiotherapy.



MM, longitudinal section of lumbar spine.

Pathophysiology and Diagnosis of Multiple Myeloma (MM)

- MM, defined by tumor accumulations of plasma cells that secrete monoclonal immunoglobulin, seems at first to be a typical disseminating hematological malignancy of mature B cells.
- 3 features defy any simplistic view likening MM to leukemias:
 - MM is widely disseminated;

- can only grow and differentiate in marrow;
- collaboration with osteoclasts, which erode bone.

•Key features for diagnosis:

--demonstration of a monoclonal immunoglobulin or the light or heavy chain in serum, and proteinuria in urine;

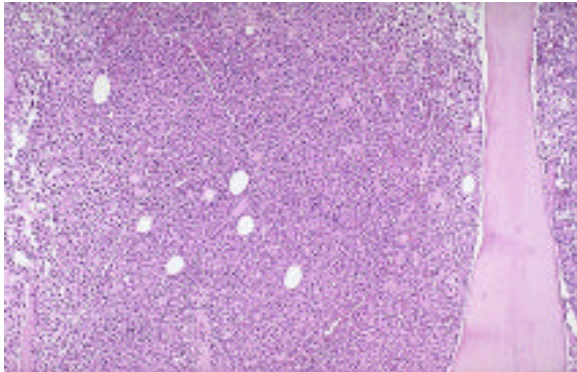
--subclass of monoclonal protein is important for prognosis.

Types of Multiple Myeloma (MM)

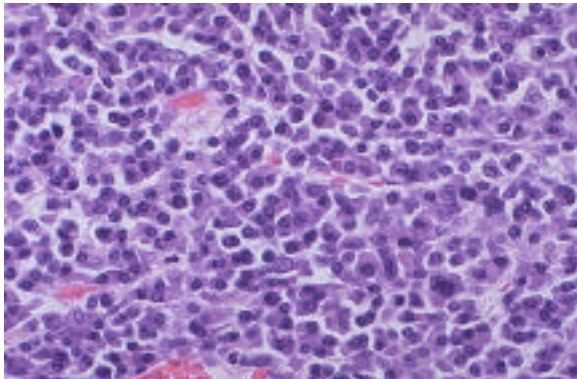
- Most MM immunoglobulins have no known specificity
- IgG myeloma is associated with slower tumor growth and lower incidence of hypercalcemia and amyloid deposits; increased susceptibility to bacterial infection.
- IgA myeloma is associated with hyperviscosity because IgA polymerizes; hypercalcemia and amyloid deposits are troublesome.
- IgD myeloma is particularly malignant; results in very sinister spleen, lymph nodes, bone tumor deposits, renal failure and amyloid deposits; survival time is about a year.
- Bence Jones (BJ) myeloma occurs when immunoglobulin light () chains are synthesized in the absence of heavy chains:
 - most rapid tumor growth and other “bad” side effects
 - prognosis grim.

Hematological Examination of Multiple Myeloma

- "Rouleaux" formation in peripheral blood.
- Bone marrow reveals presence of atypical plasma cells:
 - myeloma plasma cells
 - multinucleated cells such as "flaming plasma cells"
 - "Mott cells" are clusters of bluish, spherical-shaped cells



At low power, the abnormal plasma cells of multiple myeloma fill the marrow.



At medium power, the plasma cells of multiple myeloma here are very similar to normal plasma cells. Usually, the plasma cells are differentiated enough to retain the function of Ig production.