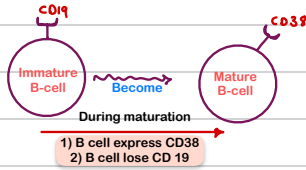


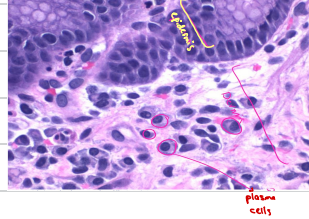
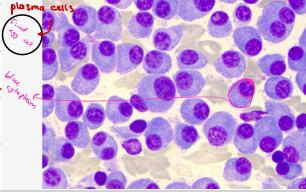
Plasma cell neoplasms and Related entities

Fast introduction 🤪:



B cell differentiates into single type of plasma cell specific against single type of Ag

specific plasma cells produce specific Antibody class against specific Ag:
 -When plasma cells are formed:
 1) **Can't switch antibody class** or change it's targeted Ag
 2) **Produce only single type of antibody** in a single class of immunoglobulin



Features of plasma cells:

- 1- Fried egg appearance
- 2- Blue cytoplasm (contains granules for immunoglobulin formation)
- 3- Eccentric nuclei
- 4- Perinuclear halo of clear cytoplasm (Golgi apparatus)
 ↳ less colored space
 ↳ rest of cytoplasm filled with antibodies and rER (basophilic)

Ex: **M protein** (monoclonal immunoglobulin)

- Found in **blood** (restricted to plasma, ECF)
- high molecular weight** (not found in urine)

find them by serum protein electrophoresis

neoplastic plasma cells

The most common and deadly example is: Multiple myeloma

monoclonal immunoglobulins
 these Ig originated from single cell, for a single Antigen, and same type.
fragments of immunoglobulins

serve as tumor markers and their increase has clinical consequences

most of clinical presentation of plasma cell neoplasm is due to Ab production

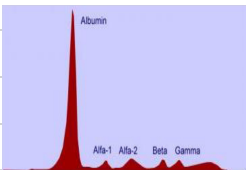
So they are used for diagnosis and follow up

EX: **Immunoglobulin light chains**

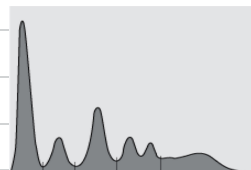
- They are **small in size**
- They can **reach urine**
- As (**Bence Jones proteins**)

find the, by urine protein electrophoresis

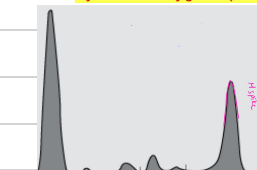
Serum protein electrophoresis



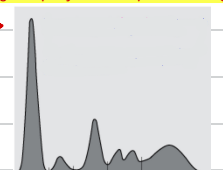
Normal serum protein
 -albumin : most abundant
 -globin : alpha, beta, gamma



Inflammation
 All types of proteins increase as many of those families has acute phase reactants and inflammation markers



Monoclonal gammopathy (M spike)
 Ig are from the same type and are against the same Ag
 1) Monoclonal in origin = all of them arised from single plasma cell type and against same Ag
 2) Monoclonal gammopathy = malignant plasma cell proliferation



Polyclonal gammopathy (Dome shaped)
 1) Polyclonal in origin = each one arise from different plasma cell
 2) Polyclonal gammopathy = benign plasma cell proliferation

If you find that only gamma proteins increased = gammopathy = increase production of Ig

Multiple Myeloma

(One of MC lymphoid malignancies)

Done by: Kareem Obeidallah

| General information | Pathogenesis | MM and renal dysfunction | Multiple Myeloma - Morphology |
|---------------------|--------------|--------------------------|-------------------------------|
|---------------------|--------------|--------------------------|-------------------------------|

Affected persons:
 -Median age 70 years
 -More common in males

IgG: the most common immunoglobulin in MM (60%)

-IgA: 2nd most common immunoglobulin in MM

-Plasma cells produce **K(kappa), λ light chains**

Most common presenting symptom is **Bone pain**

MM has a number of effects:
 جمعناهم في كلمة:
CRABI

C: hypercalcemia
R: Renal impairment (kidney)
A: Anemia
B: Bone pain and lytic lesions (skeleton)
I: Infection (immune system)

**These effects contribute to morbidity and mortality

** Involves the bone marrow and associated with lytic lesions throughout the skeletal system

Translocation mutation:
 fusion of **IgH locus on chromosome 14 to:**
oncogenes (cyclin D1 and cyclin D3 genes)

So there will be:
 1- plasma cell proliferation
 2- excessive Ig formation

MM release factors that :
 - **Upregulates** the expression of the receptor activator of NF-κB ligand (**RANKL**)

RANKL bind to RANK on osteoclast surface leading to osteoclast activation

by bone marrow stromal cells activate **osteoclasts** (potent inhibitors of osteoblast function)

increased bone resorption

Leading to:
 hypercalcemia, bone pain & pathologic fractures

Multiple Myeloma
 Compromises the function of normal B cells

Production of functional Ab is depressed

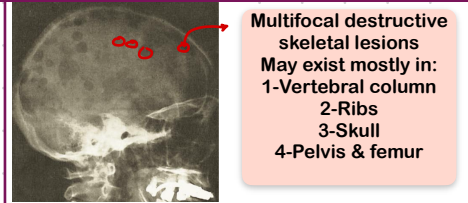
Humoral immunity is decreased, leading to: high risk for bacterial infections.

1) **Bence Jones proteins obstruct distal tubules** lead to:
obstructive proteinaceous casts

2) **Light chain deposition in the glomeruli or the interstitium**, either as amyloid or linear deposits
May contribute to renal damage.

3) **Hypercalcemia**
 lead to **dehydration and renal stones**

4) **Bacterial pyelonephritis**
 ↳ due to decrease immunity



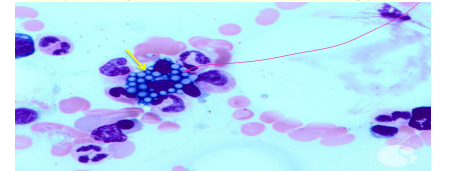
Multifocal destructive skeletal lesions
 May exist mostly in:
 1-Vertebral column
 2-Ribs
 3-Skull
 4-Pelvis & femur

▷ The lesions arise in the medullary cavity. (punched- out defects)

▷ **Bone destruction** leads to pathologic fractures. (Common 1st presentation)

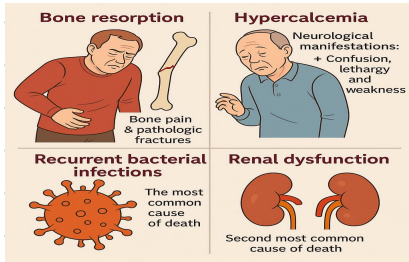


bone marrow shows:
 increased numbers of plasma cells (usually > 30% of the cellularity)



In peripheral blood
Mott cells:
 (plasma cells that have spherical inclusions packed with Ig in their cytoplasm)
 -Inclusions: **Russell bodies**-

Multiple Myeloma - Clinical Features



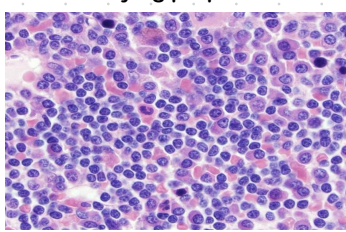
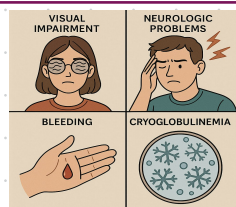
(الصورة كثير مهمة و كلها حفظ)

- ▷ Median survival is (4-7 years)
- ▷ Variable prognosis. No cure yet.

Multiple Myeloma - Laboratory analyses

- ▷ **Increased levels of:**
 - 1) **Immunoglobulins** in the blood.
 - 2) and/or **Bence Jones proteins** in the urine
- ▷ Patients have
 - Both in ~ 70% of cases
 - 20% have **only free light chains**
 - 1% of **myelomas are nonsecretory.**
- ▷ **Anemia, thrombocytopenia and leukopenia.**
- ▷ **Elevated creatinine or urea (Renal dysfunction).**

Lymphoblastic lymphoma (B cell neoplasm)

| General information | Pathogenesis | Morphology | Clinical features stemming from the physicochemical properties of IgM |
|--|---|--|--|
| <ul style="list-style-type: none"> ▷ Usually presents in old age ▷ Most commonly, the plasma cell component secretes monoclonal IgM. ▷ Hyperviscosity syndrome (Waldenström macroglobulinemia) ▷ Complications from the secretion of free light chains (e.g.; renal failure) are relatively rare & no bone destruction. <div style="background-color: #e0ffe0; padding: 5px; margin-top: 10px;"> Differences in comparison to multiple myeloma: 1- Type of Ab : IgM 2- Hyper viscosity syndrome 3- No CRABI </div> <ul style="list-style-type: none"> ▷ An incurable progressive disease ▷ Median survival 4 year | <p>associated with acquired mutations in MYD88</p> | <p>Bone marrow is: infiltrated by lymphocytes, plasma cells, & plasmacytoid lymphocytes in varying proportions</p>  | <div style="text-align: center;">  </div> <div style="background-color: #ffffe0; padding: 10px; margin-top: 10px;"> <ol style="list-style-type: none"> 1) Visual impairment: due to venous congestion & retinal hemorrhages 2) Neurologic problems (headaches, dizziness, deafness) due to sluggish venous blood flow 3) Bleeding due to formation of complexes between macroglobulins & clotting factors as well as interference with platelet function 4) Cryoglobulinemia precipitation of macroglobulins at low temperatures (Raynaud phenomenon) </div> |

Note:

Plasma Cell Neoplasms and Related Entities

Solitary plasmacytoma

An infrequent variant that presents as a single mass in bone or soft tissue

histology

- plasma cells
- no BM involvement
- no M proteins
- No CRABI

Smoldering myeloma

uncommon variant defined by: lack of symptoms and a high plasma M component

Histology

- BM involvement
- High M protein
- no CABI

Monoclonal gammopathy of undetermined significance (MGUS)

-Patients without signs or symptoms

-Small to moderately large M components in blood

** very common in older adult

** low but constant rate of transformation to MM.

Waldenström macroglobulinemia

A syndrome in which high levels of IgM

lead to symptoms related to hyperviscosity of the blood

** (Associated with lymphoplasmacytic lymphoma)

** Multiple myeloma (MM)(plasma cell myeloma)
The most important plasma cell neoplasm

Histology

- BM tumor
- high M proteins
- existing CRABI

Normal progression

MAGUS

Smoldering myeloma

Multiple myeloma