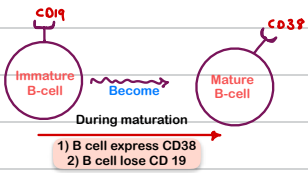
Done by: Kareem Obeidallah

Plasma cell neoplasms and Related entities

Fast introduction 😁:

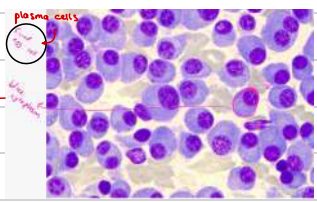


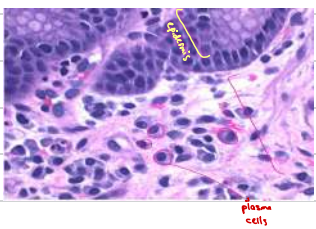
B cell differentiates into single type of plasma cell specific against single type of Ag

specific plasma cells produce specific Antibody class against specific Ag:
-When plasma cells are formed:
1)Cann't switch antibody class or change it's targeted Ag

2)Produce only single type of antibody in a single class of immunoglobulin

Contain granules that will form immunoglobulins





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 (monoclona 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

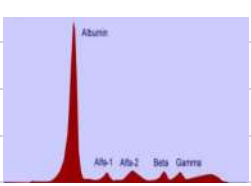
- monoclonal immunoglobulins
  these Ig originated from single cell, for a single Antigen, and same type.
- fragments of immunoglobulins

→ serve as tumor markers and their increase has clinical consequences
- So they are used for diagnosis and follow up
- most of clinical presentation of plasma cell neoplasm is due to Ab production

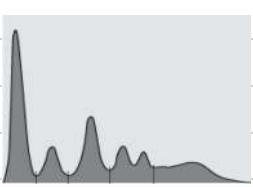
EX: Immunoglobulin light chains
-They are small in size
-They can reach urine → find the, by urine protein electrophoresis
As (Bence Jones proteins)

Serum protein electrophoresis

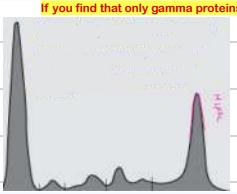
If you find that only gamma proteins increased = gammopathy = increase production of Ig



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

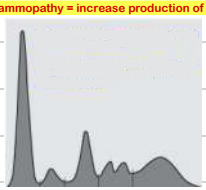


Inflammation
All types of proteins increase as many of those families has acute phase reactants and inflammation markers



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

Multiple Myeloma

(One of MC lymphoid malignancies)

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General information

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

Pathogenesis

** 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.

MM and renal dysfunction

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

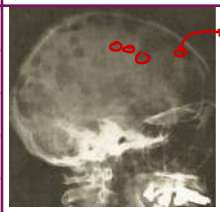
↓

lead to dehydration and renal stones

4) Bacterial pyelonephritis

↳ due to decrease immunity

Multiple Myeloma - Morphology

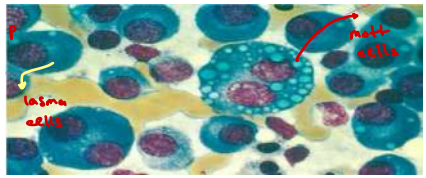


Multifocal destructive skeletal lesions
May exist mostly in:
1-Vertebral column
2-Ribs
3-Skull
4-Pelvis & femur

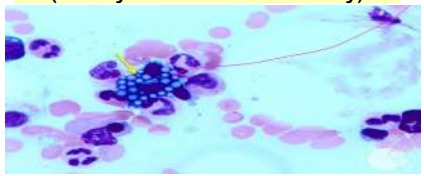
▷ The lesions arise in the medullary cavity. (punched- out defects)

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

In microscope

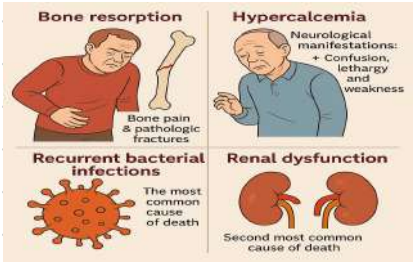


bone marrow shows:
increased numbers of plasma cells
(usually > 30% of the cellularity)



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

▷ 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.

Differences in comparison to multiple myeloma:

1- Type of Ab : IgM
2- Hyper viscosity syndrome
3- No CRABI

▷ An incurable progressive disease

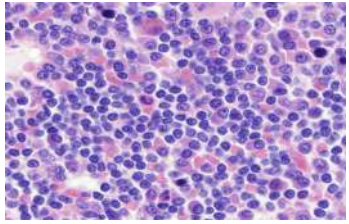
▷ Median survival 4 year

Pathogenesis

associated with acquired mutations in MYD88

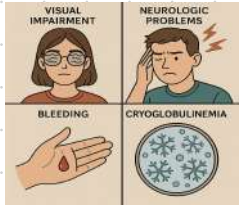
Morphology

Bone marrow is:
infiltrated by lymphocytes, plasma cells, & plasmacytoid lymphocytes
in varying proportions



Clinical features

stemming from the physicochemical properties of IgM



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)

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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

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