Plasma Cell Neoplasms and Related Entities

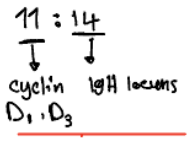
The last stage of B cell maturation, express CD38 but lose CD19:
+ cannot switch antibody classes.
+can only produce a single kind of antibody in a single class of immunoglobulin.

- B cell proliferations contain neoplastic plasma cells
- Always secrete a **monoclonal** immunoglobulin or their fragment.
- These serve as tumor markers and often have pathologic consequences.
- The most common & deadly of these neoplasms is multiple myeloma.

- **M protein**: A monoclonal immunoglobulin identified in the blood. They have high molecular weight, so they are restricted to plasma & extracellular fluid & excluded from urine.
- Neoplastic plasma cells also synthesize excess immunoglobulin light chains → smaller in size → excreted in the urine, where they are called → **Bence Jones proteins.**
- Monoclonal immunoglobulin can be detected by simple serum test → Serum protein Electrophoresis!

Plasma Cell Neoplasms and Related Entities	
Solitary plasmacytoma	infrequent variant that presents as a single mass in bone or soft tissue
Smoldering myeloma:	another uncommon variant defined by 1. lack of symptoms 2. high plasma M component.
Monoclonal gammopathyof undetermined significance (MGUS)	1. Applied to patients without signs or symptoms 2. small to moderately large M components in blood 3. MGUS is very common in older adult 4. Has a low but constant rate of transformation to MM

L ymphoplasmacytic Lymphoma(Waldenström macroglobulinemia)	
pathogenesis	acquired mutations in MYD88.
Clinical	▷Visual impairment: due to venous congestion & retinal hemorrhages ▷Neurologic problems such as headaches, dizziness, deafness, due to sluggish venous blood flow ▷Bleeding due to formation of complexes between macroglobulins & clotting factors as well as interference with platelet function ▷Cryoglobulinemiathe precipitation of macroglobulinsat low temperatures ?Raynaud phenomenon. ▷Complications from the secretion of free light chains (e.g.; renal failure) are relatively rare & no bone destruction.
Morphology	The marrow is infiltrated by lymphocytes, plasma cells, & plasmacytoid lymphocytes in varying proportions
Clinical Features.	1. An incurable progressive disease 2. Median survival 4 year
Laboratory analyses	1. hyperviscosity syndrome. : Waldenströmmacroglobulinemia a. Patients with IgM-secretingtumors have signs & symptoms stemming from the physicochemical properties of IgM b. large size -> at high concentrations IgM greatly increases the blood viscosity 2. Most commonly, the plasma cell component secretes monoclonal IgM.

	Multiple myeloma (MM)(plasma cell myeloma):
pathogenesis	1. t(11:14) ; 
Clinical	1- Bone a. Bone destruction ->the major pathologic feature of multiple myeloma. b. Multifocal destructive skeletal lesions mostly involve the vertebral column, ribs, skull, pelvis, femur. c. The lesions arise in the medullary cavity. d. Bone destruction leads to pathologic fractures. e. MM release factors that : 1. upregulates the expression of the receptor activator of NF- κB ligand (RANKL) by bone marrow stromal cells activate osteoclasts 2. are potent inhibitors of osteoblast function. {Net effect: increased bone resorption->hypercalcemia& pathologic fractures.}
	2- Humoral immunity a. MM Compromises the function of normal B cells b. production of functional antibodies often is profoundly depressed c. patients are at high risk for bacterial infections.
	3- Renal dysfunction a. obstructive proteinaceous casts; composed of Bence jones proteins in the distal tubules. b. Light chain deposition in the glomeruli or the interstitium, either as amyloid or linear deposits ->may contribute to renal damage. c. Hypercalcemia, lead to dehydration and renal stones, d. Bacterial pyelonephritis,
Morphology	1. marrow shows increased numbers of plasma cells, usually > 30% of the cellularity. 2. Mott cells are plasma cells that have spherical inclusions packed with Ig in their cytoplasm, Inclusions: Russell bodies
Clinical Features.	1. Bone resorption: Bone pain & pathologic fractures 2. Hypercalcemia: neurological manifestations; + Confusion, lethargy and weakness. 3. Recurrent bacterial infections: +The most common of death. 4. Renal dysfunction: +Second most common cause of death. 5. Median survival is 4-7 years 6. No cure yet.
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).
Note	1- The most frequent M protein produced by myeloma cells is IgG (60%), followed by IgA. 2- Plasma cells produce κ or λ light chains. 3-Principally involves the bone marrow and ass with lytic lesions throughout the skeletal system 4-Median age 70 years, more common in males. 5- The most common & deadly of these neoplasms is multiple myeloma.