HEMATOPOIETIC & LYMPHATIC SYSTEM

SUBJECT : pathology

LEC NO. : 10

DONE BY : Abdullah Harahsheh

وَقُل رَّبِّ زِدْنِي عِلْمًا

Non-Hodgkin's Lymphoma

نتذكر اول اشي عن شو حكينا المحاضرة الماضية

B-Cell Neoplasms:

- Precursor B-cell neoplasms (ALL)
- **Mature B-cell neoplasms** ➡

✅ حكينا عن ال intermediate and low
✅ وحكينا عن اول نوع بال high
اليوم رح نحكي عن ثاني نوع

HIGH GRADE B CELL NHL

1. Diffuse Large B-cell Lymphoma (DLBL)

اي اشي جنبه 🚨 ..... مهم
اي اشي جنبه ❌ ... الدكتورة ما ذكرته

2. Burkitt Lymphoma

ممكن ما يكون عنده اشي ،فجأة بصير عنده كتلة وبتتضاعف بسرعة

- It is a highly aggressive and rapidly proliferating lymphoma.

Three major types exist:

1. African (endemic).
2. Western (non-endemic, sporadic).
3. Immunodeficiency associated.

ميزة لهلنوع (🚨مهم)

- Both the endemic and nonendemic forms affect mainly **children and young adults**.

برا ال lymph node ، بصيروا بأي مكان

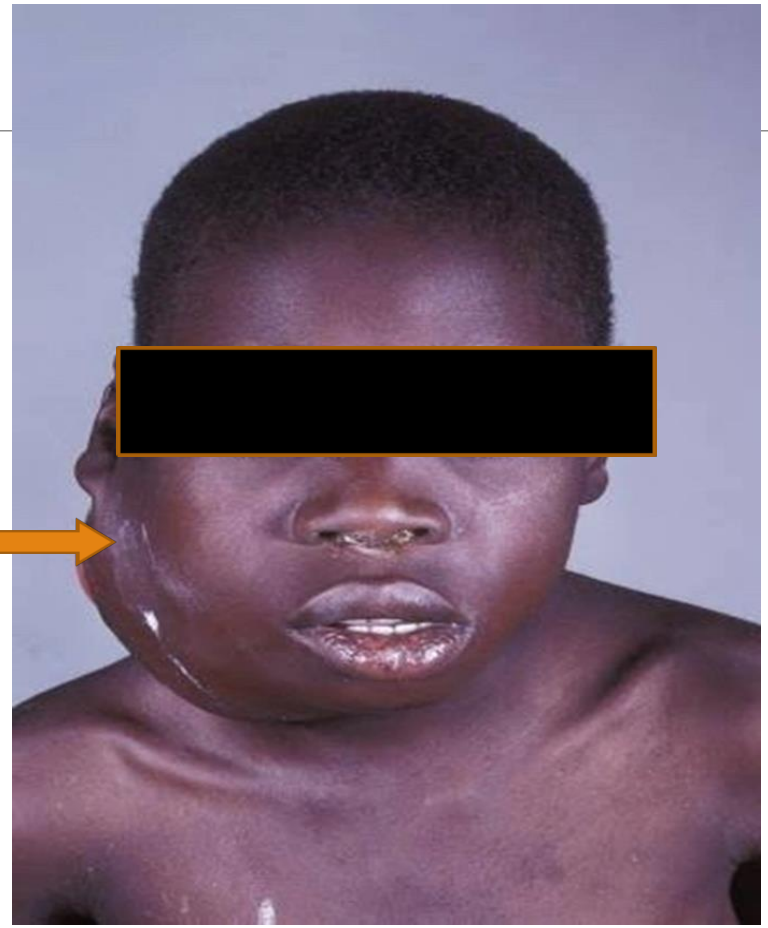
- In both forms, **the disease usually arises at extranodal sites**. 🚨

منطقة الوجه

- In **African** patients, involvement of the **maxilla or mandible** is the common mode of presentation.
- In **North America, abdominal** tumors involving the bowel, retroperitoneum, and ovaries are more common

❑ Pathogenesis

- In most of African Burkitt's lymphoma, tumors carry the **EBV** genome.
- In ~20% of sporadic cases, the EBV genome is found in the tumor cells.
- Burkitt's lymphoma show **t(8;14)** chromosomal translocation(involves the **MYC** gene)



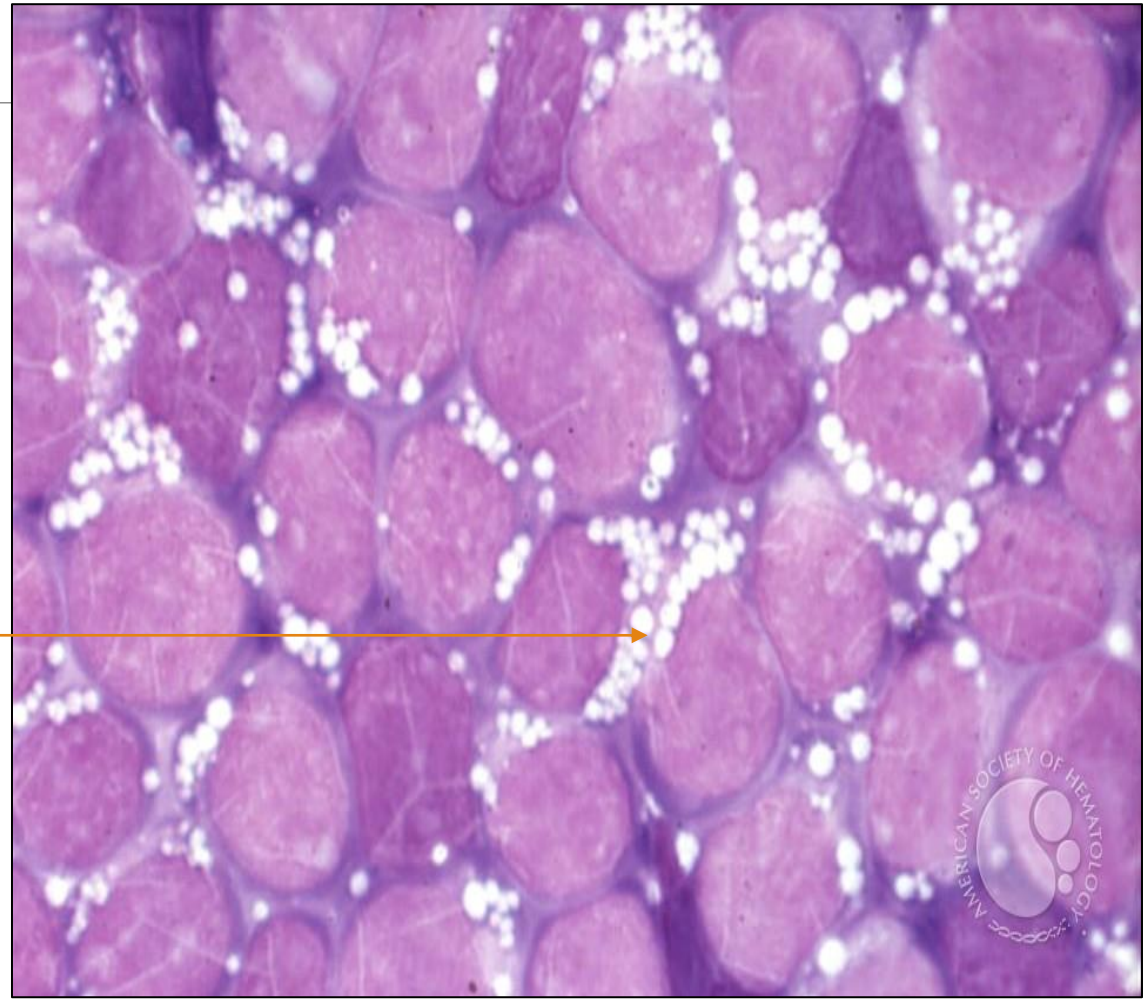
Endemic Burkitt Lymphoma in the jaw among African children.

Morphology

- **Diffuse** growth pattern. monotous

- The tumor cells are uniform and **intermediate** in size and typically have round or oval nuclei with 2-5 distinct **nucleoli**.

- There is a moderate amount of basophilic or amphophilic cytoplasm that often contains small, **lipid-filled vacuoles** (a feature appreciated on smears). 🚨

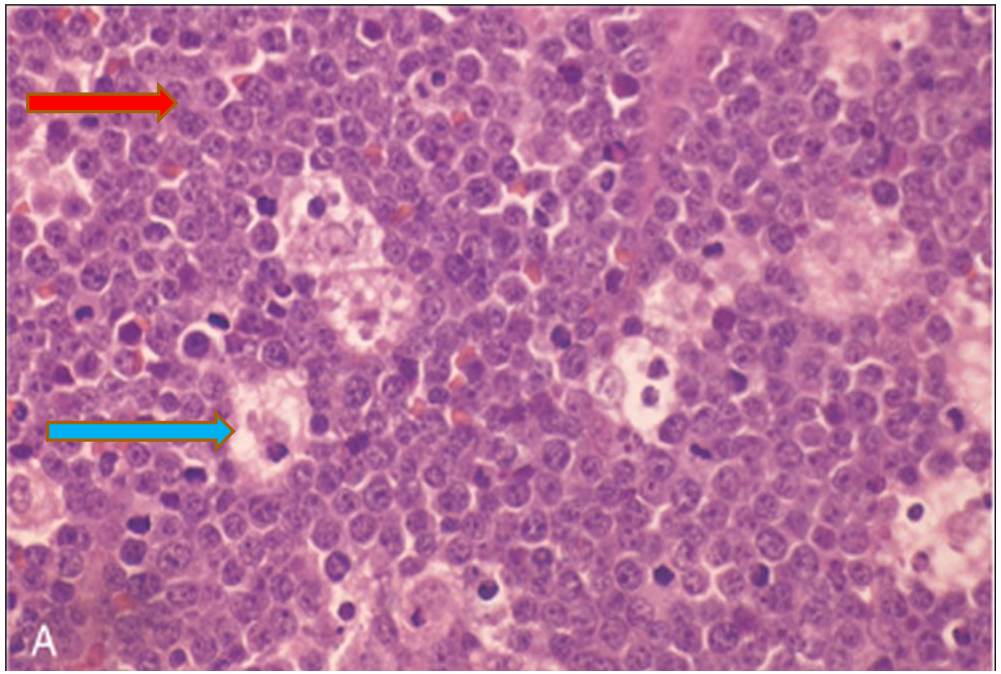


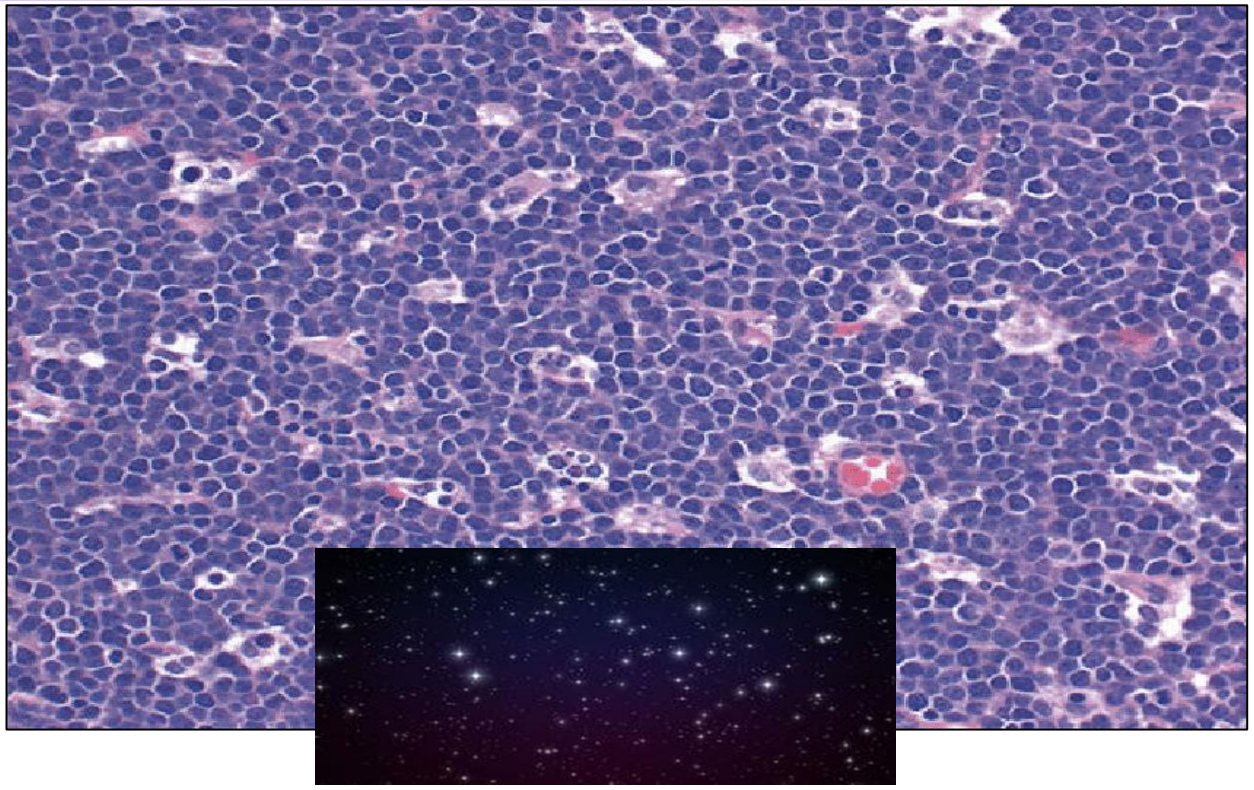
هسا مش بصير فيه تكاثر للورم بسرعة ؟ وفي خلايا بتموت اكيد
مين بده يومل هالخلايا ؟ الماكروفيج وبكون لونها فاتح

Diffuse sheets of medium sized neoplastic lymphocytes with abundant mitosis and apoptotic bodies, beside tingible body macrophages

- **A high mitotic rate** is very characteristic of this tumor, as is cell death accounting for the presence of numerous tissue **macrophages** containing ingested nuclear debris.
- Because these benign macrophages are often surrounded by a clear space, they create a" **starry sky**" pattern.

neoplastic lympho+ mammamacrophage+ high mitosis مؤلف من





❑ Immunophenotype:

- These tumors express the B cell marker CD20.

❑ Prognosis

في امل من علاجه

- Burkitt lymphoma is highly aggressive; however, with very intensive chemotherapy regimens, most patients can be cured.

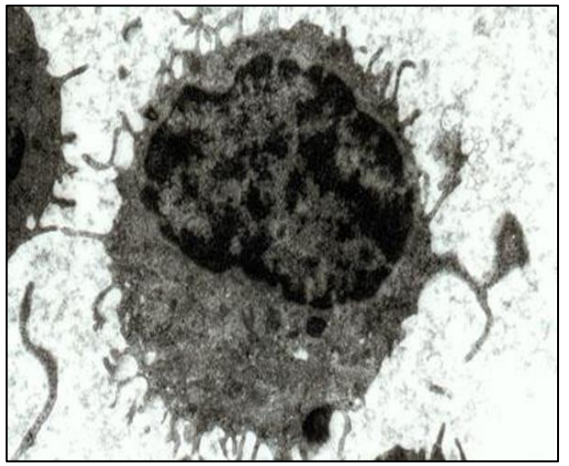
Hairy Cell Leukemia

Low-grade neoplasm

tumor of B cell

زاوئد على السيتوبلازم

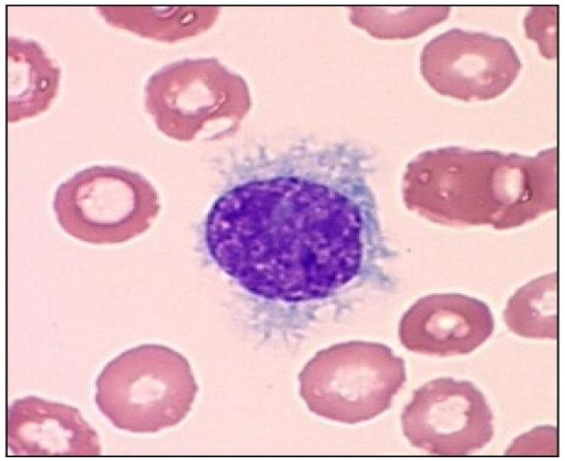
- It is a rare indolent B-cell neoplasm characterized by the presence of fine, hairlike cytoplasmic projections.



- Middle-aged males

- **Massive splenomegaly.**
- **Pancytopenia** due to BM infiltration.
- **Lymph node** involvement is **rare**.
- **> 90%** have point mutations in the **BRAF** gene.
- Distinctive markers: B cell markers, **CD11c, CD25, CD103.**
- **Indolent course** with **excellent response** to chemotherapy

بتكون بوسيتيف اكثر اشي الهم

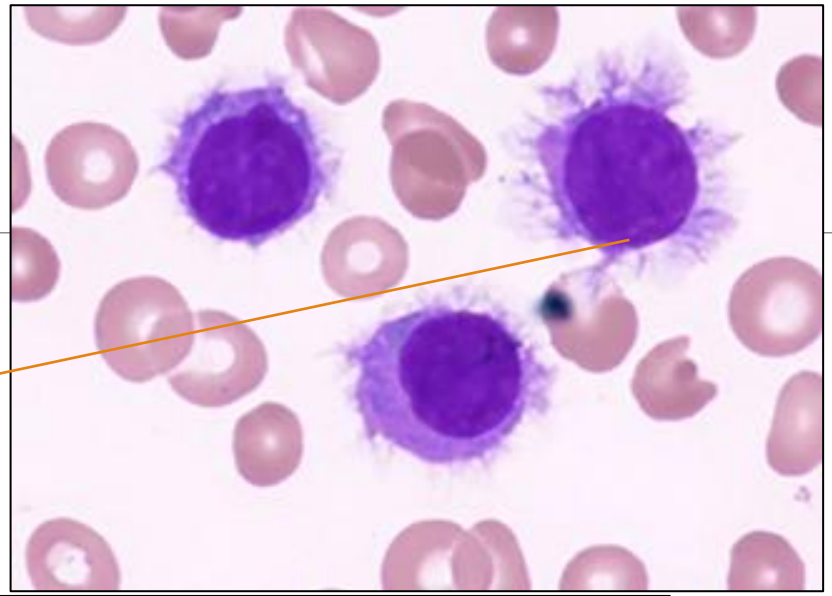


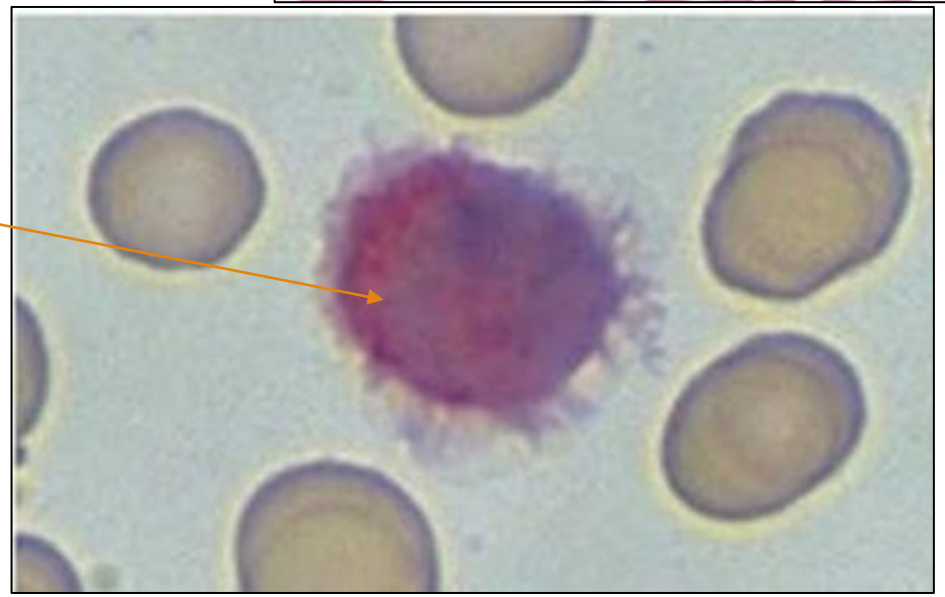
مهم نعرف اللي مخطط عليهم

Microscopic

- Peripheral blood smear shows abnormal lymphocytes with indistinct cytoplasmic borders and surface projections, giving the cells a "**hairy" appearance**.
- The red cytoplasmic staining seen at the lower right is **tartrate-resistant acid phosphatase (TRAP) positivity**

هو انزيم

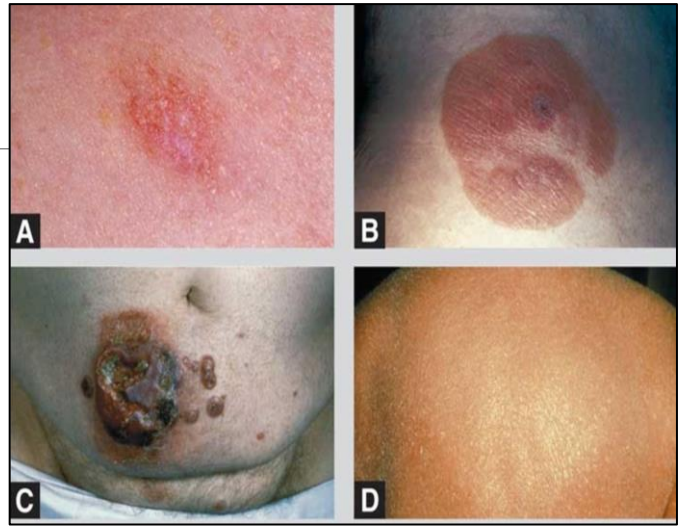




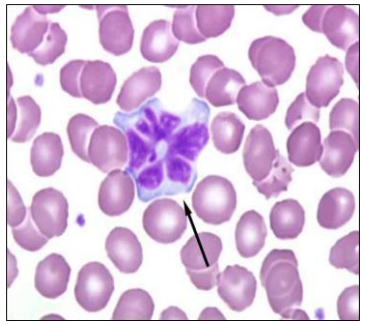
T-cell lymphoma/Leukemia

المريض بيجي وعليه skin lesion احنا بنفكره التهاب بس هو ورم

مثال عليه



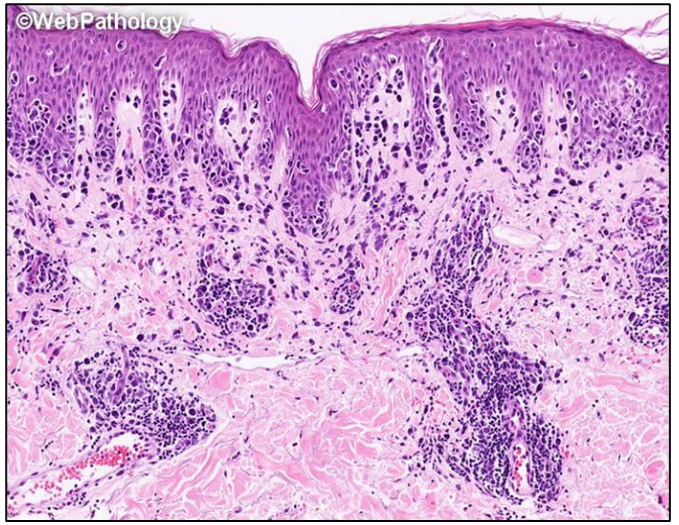
❖ Mycosis Fungoides



- Cutaneous T-cell lymphoma, usually CD4+

- Erythema, plaque, and tumor phases

- Epidermis and dermis infiltrated by cerebriform cells with marked infoldings of the nuclear membranes.



الدكتورة حكت مش مهم نعرف ال morphology اله المهم نعرف انه skin lesion

نوع ثاني

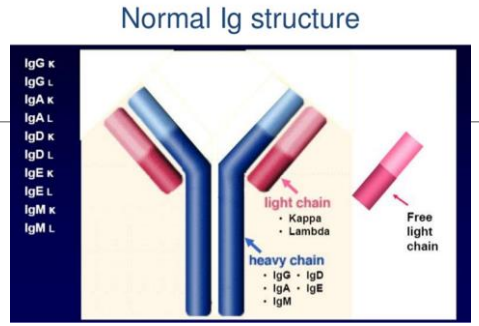
❖ Adult T-cell Leukemia/Lymphoma

- Neoplasm of **CD4+** T cells
- Infection by **HTLV-1** مصعب مع هالفيروس
- Skin lesions, generalized Lymphadenopathy, hepatosplenomegaly, hypercalcemia.
- Very aggressive

بس اعرف انه بصاحبها هالفيروس: Human T-cell Lymphotropic Virus

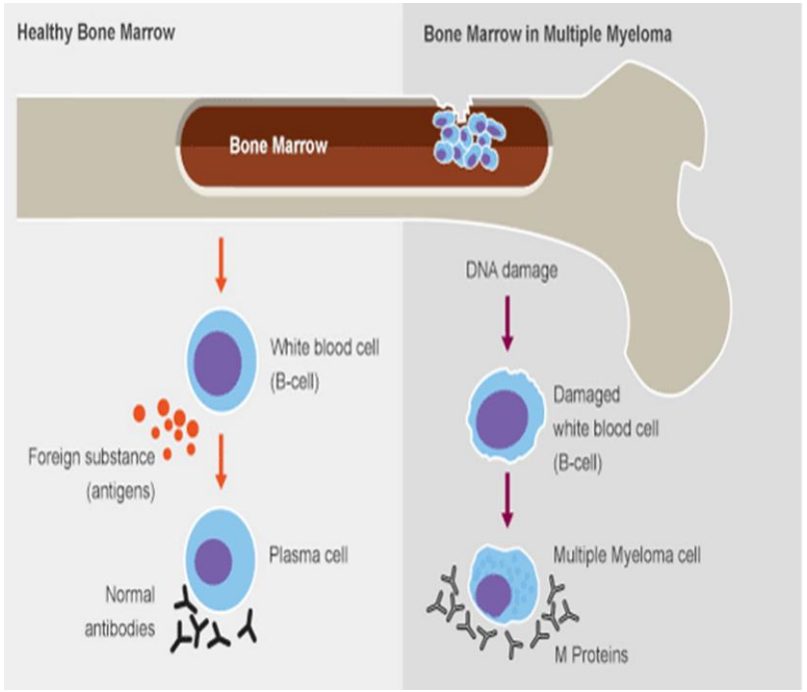
هو tumour مكون من plasma cell وهي malignant

Plasma Cell Neoplasms



- Expansion of a single clone of immunoglobulin-secreting cells with serum increase of a **monoclonal Ig "M component," monoclonal gammopathy**

- B cell proliferations contain neoplastic plasma cells that secrete a monoclonal immunoglobulin or immunoglobulin fragment.



ال B cell بصيرلها differentiation ل plasma cell وال plasma بتعطينا antibody لتشتغل في المناعة
وال immunoglobulin= anti مكون من heavy chain بنعطيها اسماء زي ال IgG,IgA
وال light chain بتكون kappa or lambda
طيب هيك ال plasma cell المفروض تفرز anti بس لانه فيها ورم بتصير تفرز monoclonal immunoglubin او ال M component وهمّي abnormal
ومش شرط تنتج خلايا البلازما كل ال anti ممكن تنتج جزء منه يعني ممكن تعطي light chain فقط

Plasma cell neoplasm classification

مش مطلوب ،فقط ١+٢+٣

WHO CLASSIFICATION OF PLASMA CELL NEOPLASMS
Non-IgM monoclonal gammopathy of undetermined significance (precursor lesion)
Plasma cell Myeloma • Smouldering plasma cell myeloma • Non-secretory myeloma • Plasma cell leukemia
Plasmacytoma • Solitary plasmacytoma of bone • Extramedullary plasmacytoma
Monoclonal immunoglobulin deposition diseases • Primary Amyloidosis • Systemic light and heavy chain deposition diseases
Plasma cell neoplasms with associated paraneoplastic syndrome • POEMS syndrome • TEMPI syndrome (Provisional entity)

1. **Multiple myeloma (plasma cell myeloma).** اهم واحد
2. **Lymphoplasmacytic lymphoma (Waldenström macroglobulinemia).**
3. **Monoclonal gammopathy of undetermined significance (MGUS)**

Multiple Myeloma

مميت ،ممكن المريض يودعنا بسببها

- The most common and deadly of these neoplasms.
- It is a B-cell neoplasm.
- It is a clonal proliferation of neoplastic plasma cells in the **bone marrow** that is usually associated with a **multifocal lytic lesions** throughout the skeletal system (commonly involve the **vertebral column**, ribs, skull, pelvis, femur, clavicle).

بتكون بأكثر من مكان في جهازه العظمي

- The median age is 70 years, M >F

الدكتورة حكت نعرف اهم نوع ممكن ينتج ،ال most common وهوال IgG

- Malignant plasma cells secrete complete immunoglobulin molecules called: M protein, which is IgG (60%), IgA (20% to 25%)and,

تنتج جزء واحد

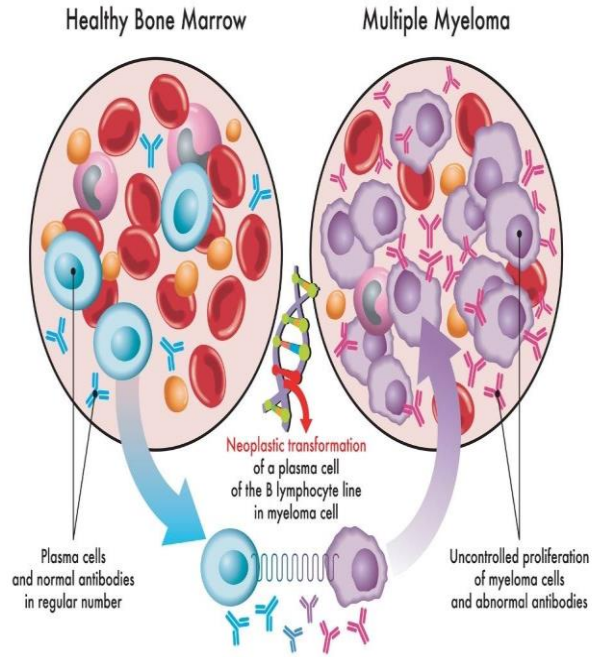
- In the remaining cases, the plasma cells produce only κ or λ light chains, the free light chains, because of their low molecular weight, are rapidly excreted in the urine called: Bence - Jones proteins.

تعمل مشاكل بالكلية

اعرف اللي مخطط عليه بس

Pathogenesis

- Myelomas have chromosomal translocations involving the **IgH** locus(chr**14).**
- The fusion partners include the **cyclin D1**, **FGFR3**,and **cyclin D3** genes.
- Dysregulation of D cyclins is believed to contribute to increases in cell proliferation
- Plasma cells in multiple myeloma are supported by the cytokine **IL-6,** which is produced by fibroblasts and macrophages in the bone marrow stroma.



Translocation affecting cycling D1 or D3

عندهم ورم وبتكاثر جوا العظم

Clinical features

لانه خلايا البلازما بتفرز cytokines معينه بتحف وبتحت بالعظم ف بطلع منه كاليسيوم

- Bone pain and fractures: Resulting from bone resorption.

مش صاحي على حاله

- Hypercalcemia: Resulting from bone resorption ⟶ neurological problems (confusion, weakness) and renal dysfunction
- Recurrent infections: due to marked suppression of normal humoral immunity.
- Anemia and bleeding: due to replacement by tumor cells with suppression of hematopoiesis.

بسبب خروج ال light chain من قنوات الكلية ف بتترسب

- Renal insufficiency: result from the effects of **Bence Jones protein (**Obstructive proteinaceous casts),

Light chain deposition, as amyloid, renal stones, Bacterial pyelonephritis

ممكن يعمل infection بالكلية برضو بسبب الCa العالي

- AL-type **amyloidosis**

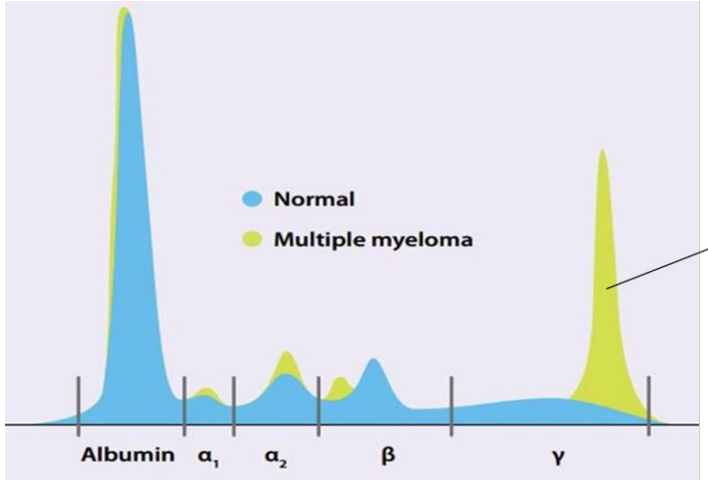
Diagnosis

multiple myloma لازم ينطبقوا ال ٣ شروط على المريض حتى نعتبر انه معه

1. Demonstration of monoclonal plasma cells in the bone marrow

   (≥ 10%).

2. Monoclonal proteins in the serum.
   abnormal immunoglobin
3. End organ damage, defined as:
   i. HyperCalcemia
   ii. Renal dysfunction
   iii. Anemia (CBC)
   iv. Lytic Bone lesions (X-ray) → Multiple bone lesions

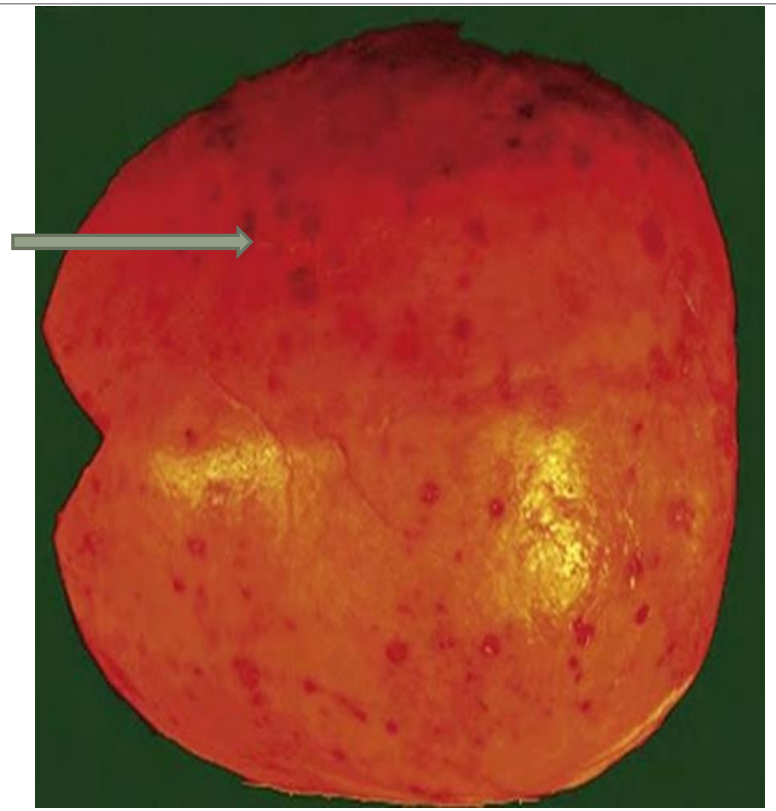


➢ Remember: CRAB (Calcium, Renal, Anemia, Bone)

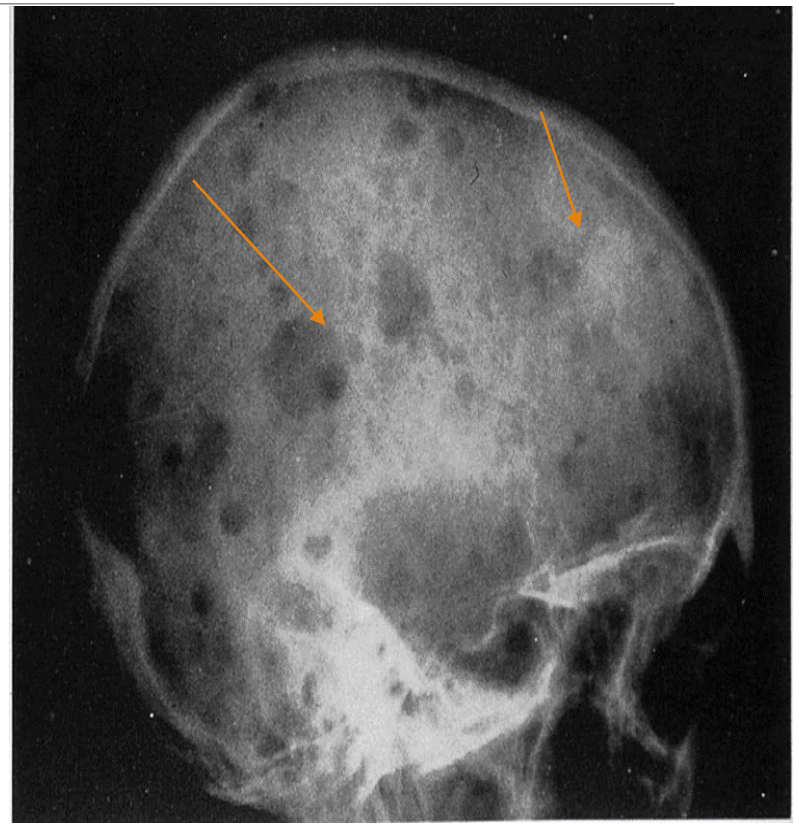
بسبب الحف والحت

Grossly:

- This skull shows the characteristic rounded "punched-out" defects due to plasma cell proliferation resulting in bone lysis.



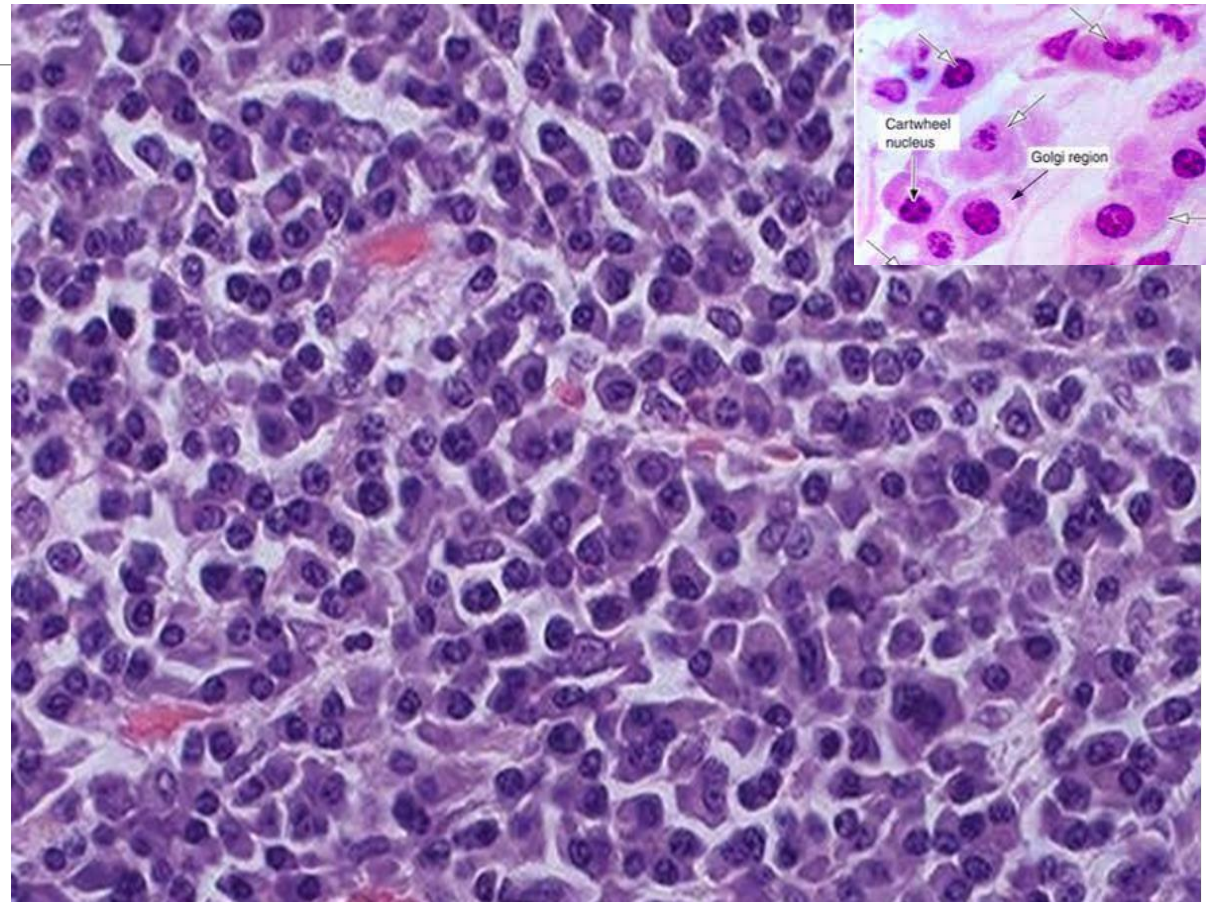
Skull X-ray showing multiple "punched out" osteolytic lesions



Microscopically:

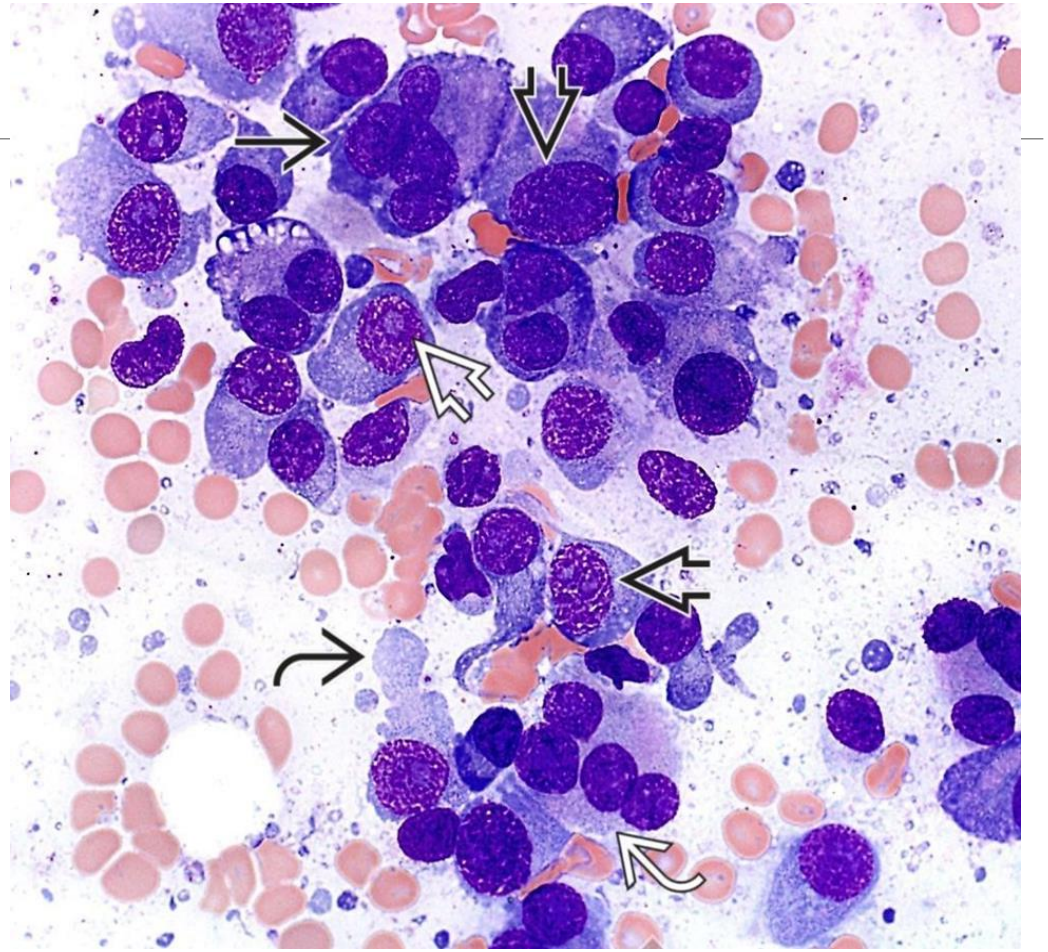
In the bone marrow biopsy section: there are sheets of plasma cells that are very similar to normal plasma cells, with eccentric nuclei and abundant pale purple cytoplasm resembling bike wheel.

بتكون على جنب



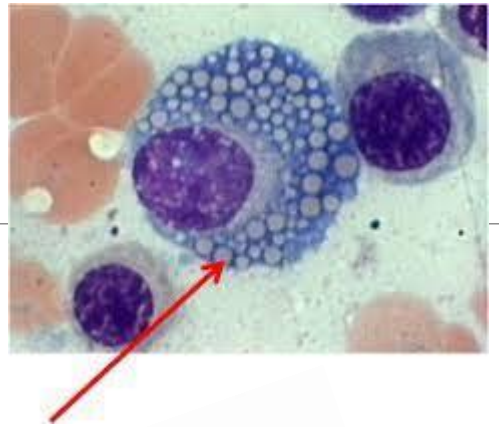
Dysplastic featureنفس

- Features of PC atypia are illustrated in this aspirate, including:
  - Cellular and nuclear enlargement, nuclear pleomorphism (black solid arrow),
  - Multinucleation (white curved arrow),
  - Dispersed nuclear chromatin (black open arrow),
  - Prominent nucleoli (white open arrow)
  - Cytoplasmic fraying or shedding(black curved arrow).

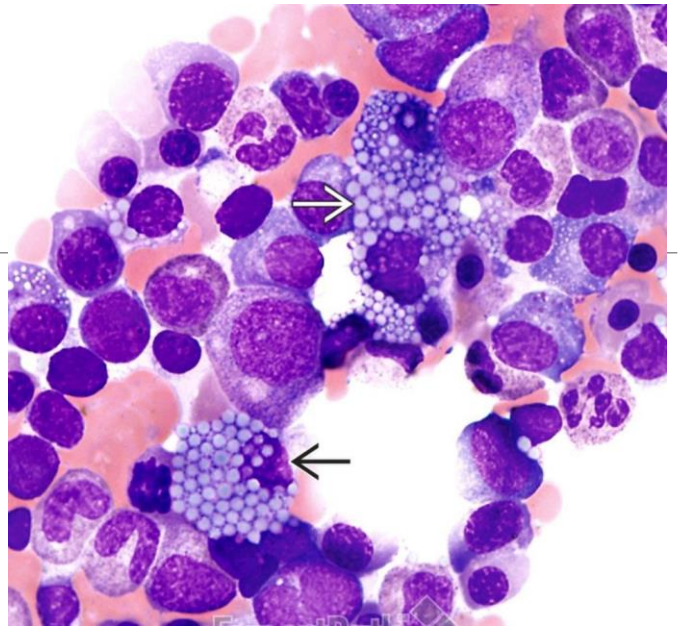


ممكن يتجمع ال imm داخل ال PC

- Immunoglobulin accumulations appear as uniform, round, colorless globules called **Russell bodies** (white solid arrow) in the cytoplasm.

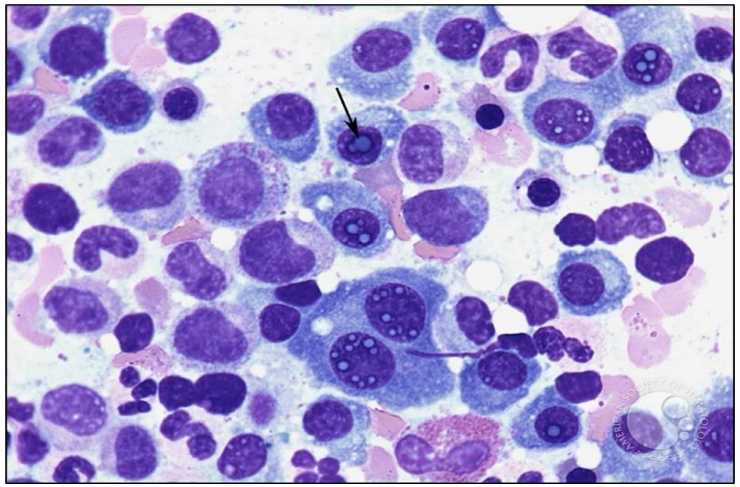


- When multiple Russell bodies are in the cytoplasm of cells, they are referred to as **Mott cells or morula cells, grape-like cells** (black solid arrow).



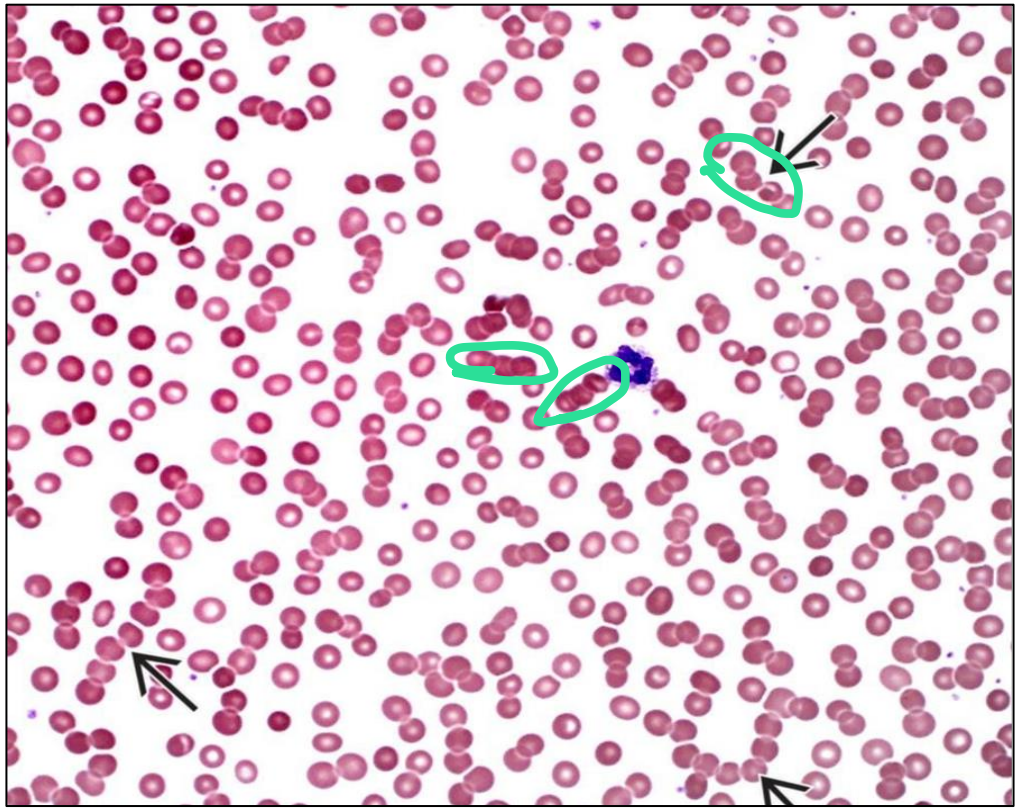
- If the inclusions are intranuclear they are called: **Dutcher bodies** (black arrow)

داخل النواة



Peripheral Blood

- **Rouleaux** formation (black solid arrow) is the linear arrangement of ≥ 4 red cells that resembles a stack of coins.
- It indicates increased proteins in the blood (i.e., Ig in myeloma)

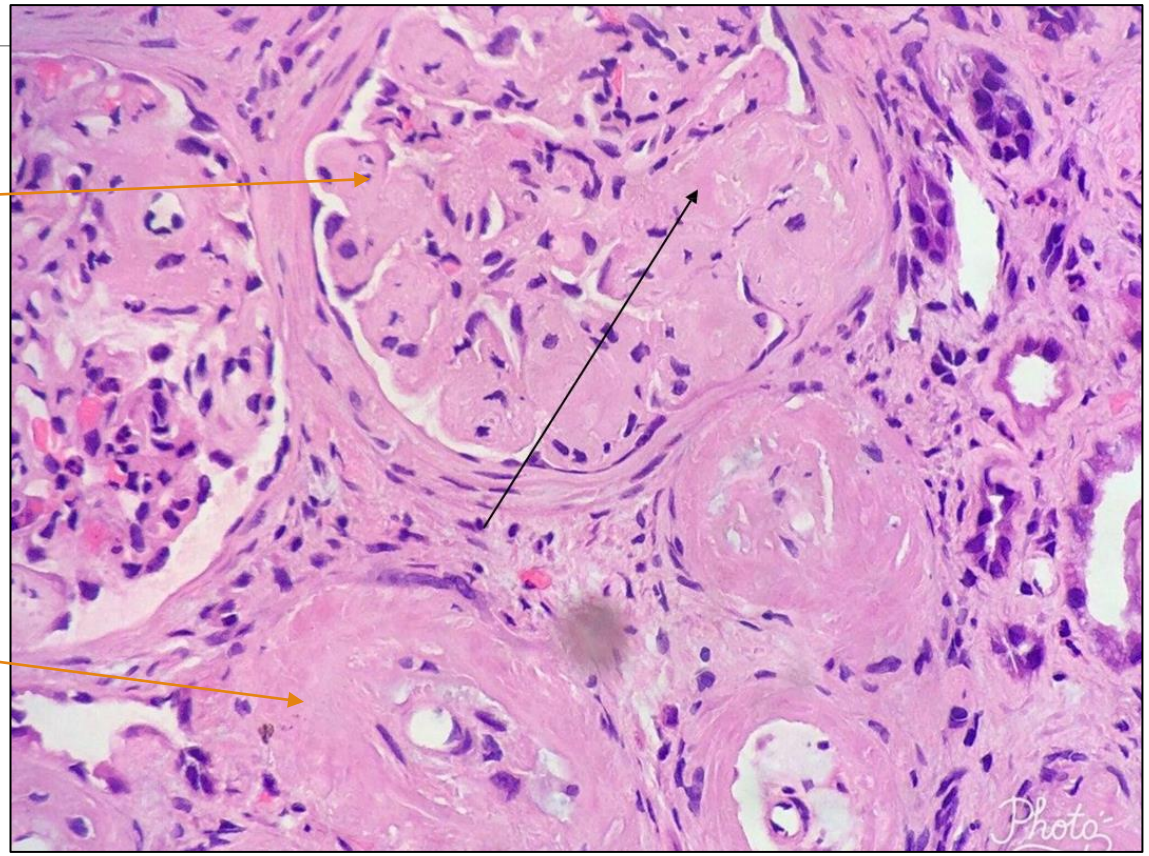


بصير احيانًا deposition لل light chain على شكل ال amyloid
بكون على شكل pink وما فيها كثير خلايا ، ممكن نشوفها بالكلية وال BV

Renal Amyloidosis, Multiple Myeloma

- In the renal cortex, pale pink amyloid deposits are visible within glomeruli.

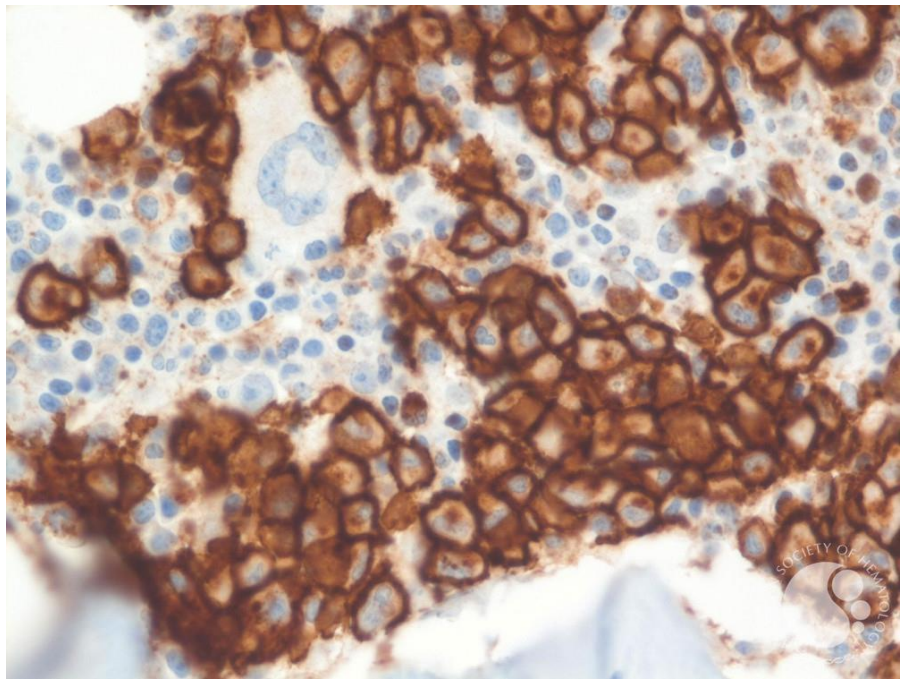
- The **amorphous pink deposits of amyloid** may be found in and around arteries, in the interstitium, or in glomeruli.



Immunophenotyping

هسا احنا بنفكر لانه ال PC جاية من ال B cell بتكون positive لل B cell markers بس لأ
بتوخذ ماركر ثاني وهو مش كثير مهم

- Despite it being a B-cell neoplasm, it does not express B-cell markers.
- It expresses CD138, and monoclonal kappa or lambda light chain.



Prognosis

- Variable.
- If untreated, patients rarely survive for more than 6 to 12 months
- The median survival is 4 to 7 years.

حسب العلاج

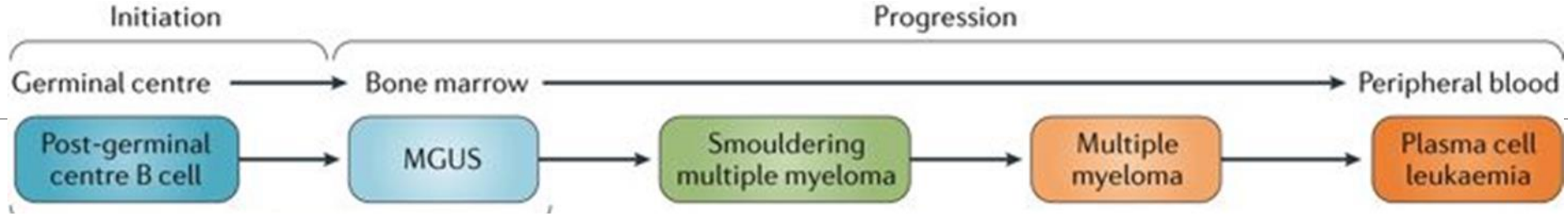
خلصنا من اهم نوع

مرضى مش مبين انه عندهم مرض

Monoclonal Gammopathy Of Undetermined Significance (MGUS)

- M proteins are found in the serum of 1 % to 3 % of asymptomatic healthy persons older than age 50 years, making this the most common plasma cell proliferation.
- M-protein <3 gm/dl بالدم
- Clonal PC's in BM **<10%**
- No symptoms of myeloma present
- Risk of progression to myeloma is 1 % per year

ممكن تتطور حالتهم ل multiple myeloma



ما عنده اعراض ،بس لما عملنا تحليل للدم بين معنا الاتي

MGUS

Monoclonal protein spike <3 g/dL

Plasma cells (PC) <10% of bone marrow

No CRAB features

Smouldering multiple myeloma

Monoclonal protein spike >3 g/dL زادت

PC >10% of bone marrow

No CRAB features

بس برضو فش اعراض

زادت

Multiple myeloma

Monoclonal spike

PC >10% or plasmacytoma

CRAB features

Or PC >60% or SFLC ratio >100

Or more than one focal lesion on MRI

ورم بال lymph node، مكون من lymphoid cells + PC

Lymphoplasmacytic lymphoma

- B cell neoplasm,

- In 6^{th}-7^{th} decades. adult

الدكتورة ذكرت بس المخطط

🚨 A substantial fraction of the tumor cells undergo differentiation to plasma cells. Most commonly, the plasma cell component secretes monoclonal **IgM**, often in amounts sufficient to cause a hyperviscosity syndrome known as **Waldenström macroglobulinemia**.

لانه حجمه كبير ف بزيد لزوجه الدم

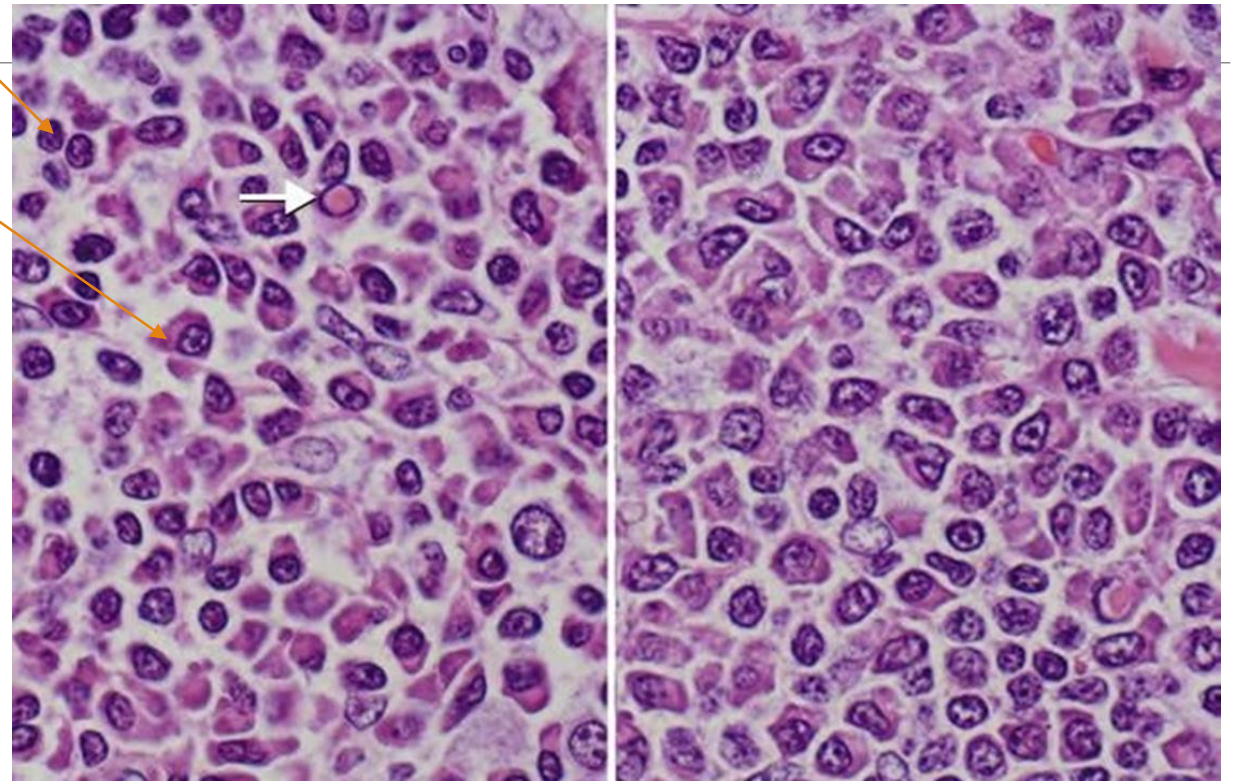
- Acquired mutations in MYD88 encoding part of the NF-κB signaling pathway are nearly always present.

Microscopically

sheet of cell

The **marrow** contains an infiltrate of lymphocytes, plasma cells, and plasmacytoid lymphocytes in varying proportions.

PAS-positive inclusions containing immunoglobulin are frequently seen in the cytoplasm **(Russell bodies)** or the nucleus **(Dutcher bodies) (white arrow).**



Clinical Symptoms

- Weakness, fatigue, and weight loss.

- Lymphadenopathy, hepatomegaly, and splenomegaly.

- Anemia caused by marrow infiltration is common.

- About 10% of patients have *autoimmune hemolysis* caused by IgM.

🚨 Excess **IgM** secretion in the blood leads to a hyperviscosity syndrome (Because of its large size), with clinical features including:

- Visual impairment — الدم رح يصير بطيء باماكن معدده منها : ocular vein بالعين
- Neurologic problems: Headaches, dizziness, deafness
- Bleeding. ممكن ال IgM يأثر على ال platelets ويمنعها من انها تشتغل

  - Lymphoplasmacytic lymphoma is an incurable, progressive disease
  - Median survival is about 4 years. ال prognosis تبعها سيء

الدكتورة اكدت على ال multiple myloma وحكت اهم اشي نعرفه

صلاة التراويح من أرض العزة

يُرِيدُونَ لِيُطْفِئُوا نُورَ اللَّهِ بِأَفْوَاهِهِمْ وَاللَّهُ مُتِمُّ نُورِهِ وَلَوْ كَرِهَ الْكَافِرُونَ

اللهم إنّا نستودعك أهل غزة ، اللَّهُم كُن لهم عونًا، اللهم إنّا لا نملك لغزة إلا الدعاء فيارب لا ترد لنا دعاء ولا تخيب لنا رجاء وأنت أرحم الراحمين ...

اللهم احفظ فلسطين وأهلها .. اللهم كن لأهلنا هناك عونا ومعينا .. وللمسجد الاقصي حافظا واامينا .. اللهم إنا نستودعك غزة فأحفظها بحفظك يا خير الحافظين ...

تذكروهم في صلاة التراويح والقيام واهلنا في السودان