INTERESTING HEMATOLOGY CASE

- Dr Vaishali Dhanke (JR1)
- Dept of Pathology
- Dr Dy Patil Medical College, Hospital and Research Centre, Pimpri.

CASE PROFILE

- 69 year old female.
- Came with complaints of back and right thigh pain since 1 month and difficulty in weight bearing, similar complaints started in left thigh.
- K/C/O - HTN and Type II DM since 2016.
- O/E :

  BP - 140/90 mmHg

  PR- 82/min.

  SPO2 - 94% RA.

LAB FINDINGS

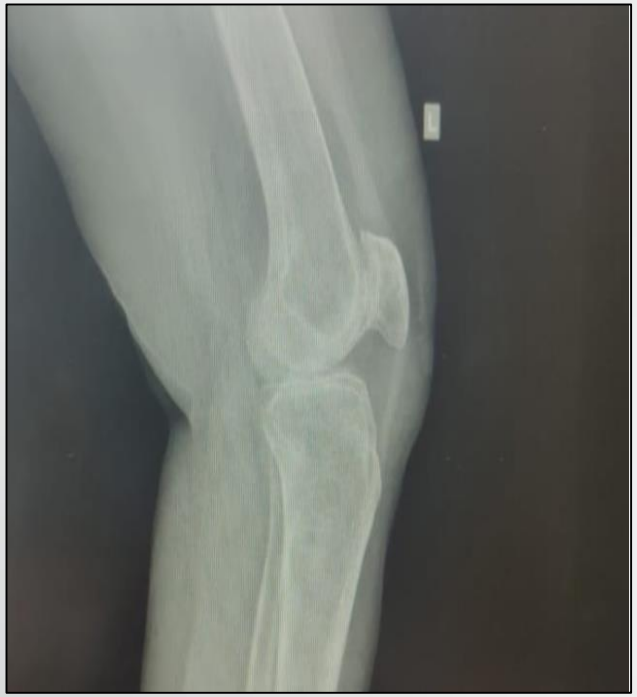
CBC

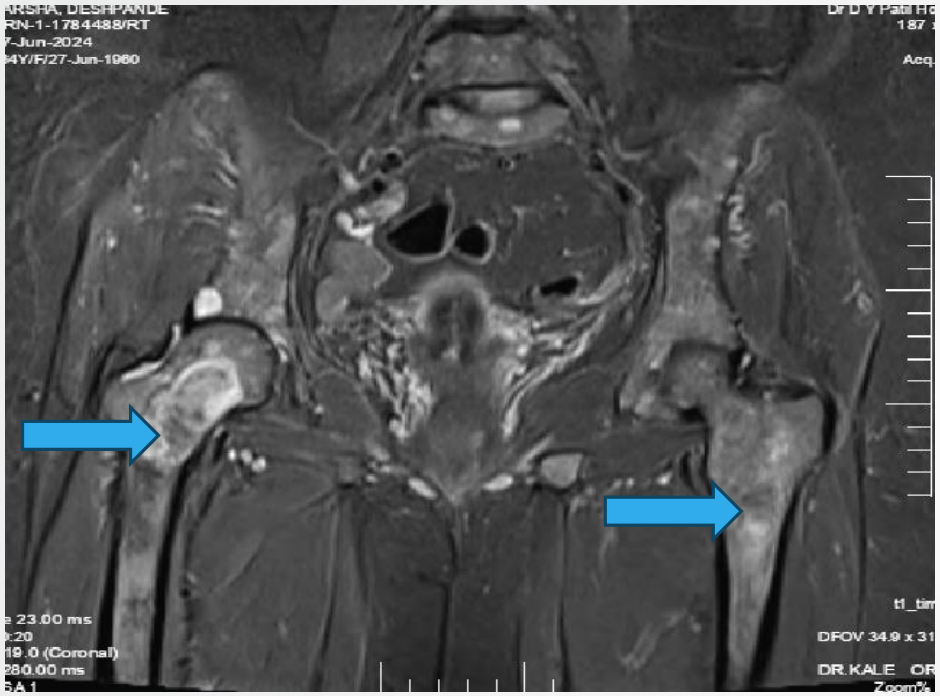
- **RBC – 3.54 x 10^6/ µL**
- **Hb – 9.4 gm/dl**
- MCV – 82.1fL
- **RDW 17.9**
- TLC – 5.9 x 10^3 / µL
- Platelet count – 251 x 10^3/ µL
- MPV – 7.9fL

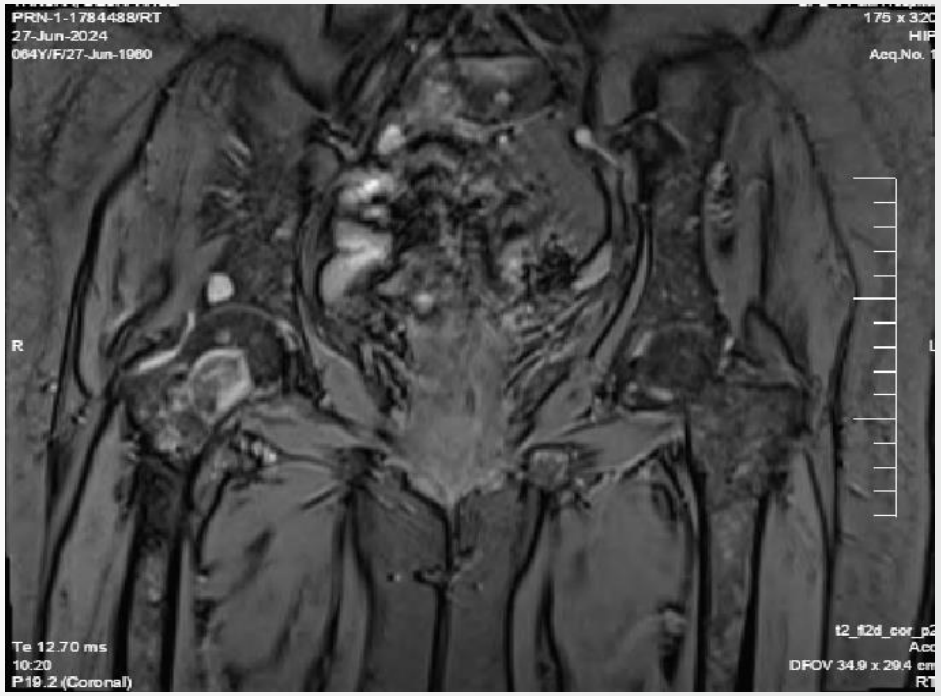
BIOCHEMISTRY

- Serum creatinine – 0.66 mg/dl. (N)
- Serum CRP – 0.19 mg/l (N)
- **ESR – 94 mm/hr (↑)**
- **Total protein- 10.10 g/dl (↑)**
- Serum albumin – 3.60 g/dl (N)
- **Serum globulin – 6.5 g/dl (↑)**
- A:G ratio – 0.55 (reversed)
- **Bence Jones proteins - Not detected**

RADIOLOGICAL INVESTIGATIONS







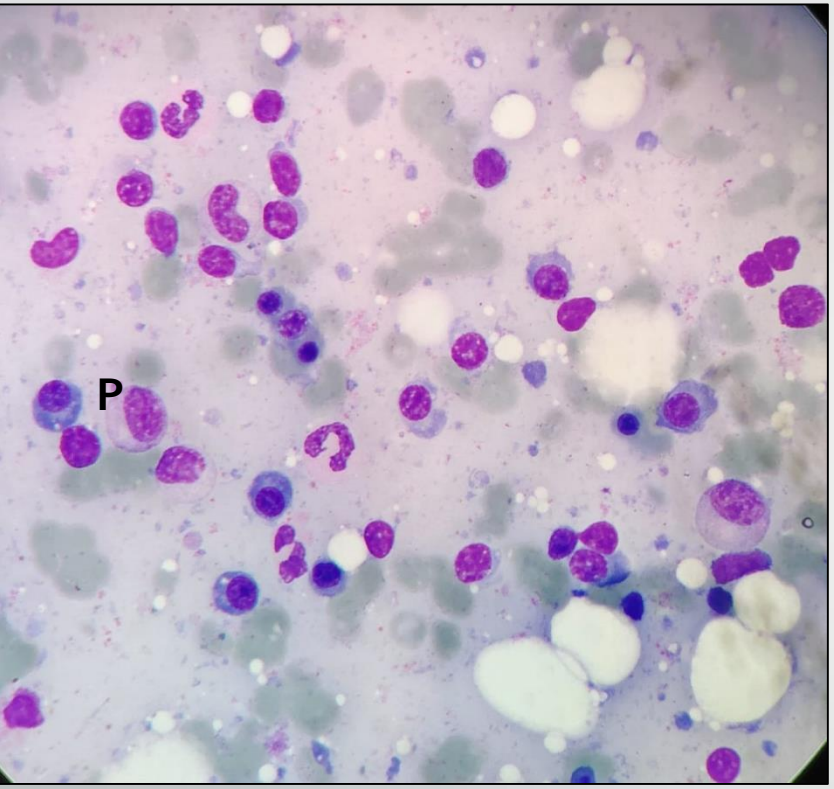
➢ **X – Ray** : Osteoarthritis of both knee joints.

➢ **MRI** : Well-defined mixed intensity lesions in the neck of right femur and postero - inferior aspect of the right side of sacrum.

Differentials include : multiple skeletal metastasis and marrow infiltrative disorder.

➢**PET- CT** : Multiple metabolically active marrow and lytic skeletal lesions involving axial and appendicular skeleton.

BONE MARROW ASPIRATION



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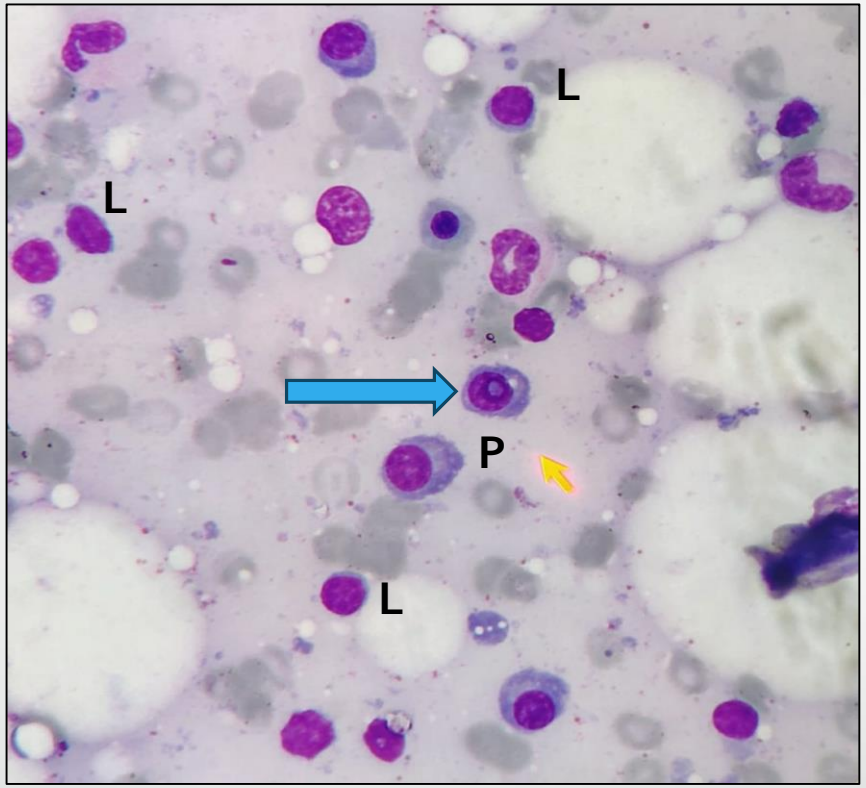

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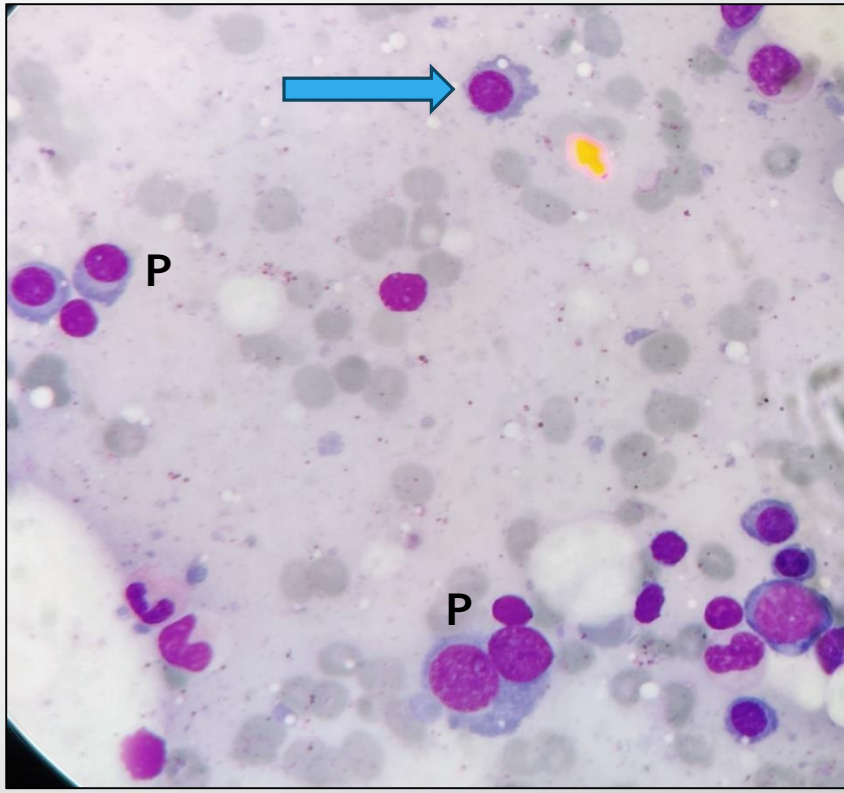


C

A- (40x) : Leishman stained bone marrow aspirate shows hypercellular bone marrow with (10%) mature and immature plasma cells and mildly increased lymphocytes.

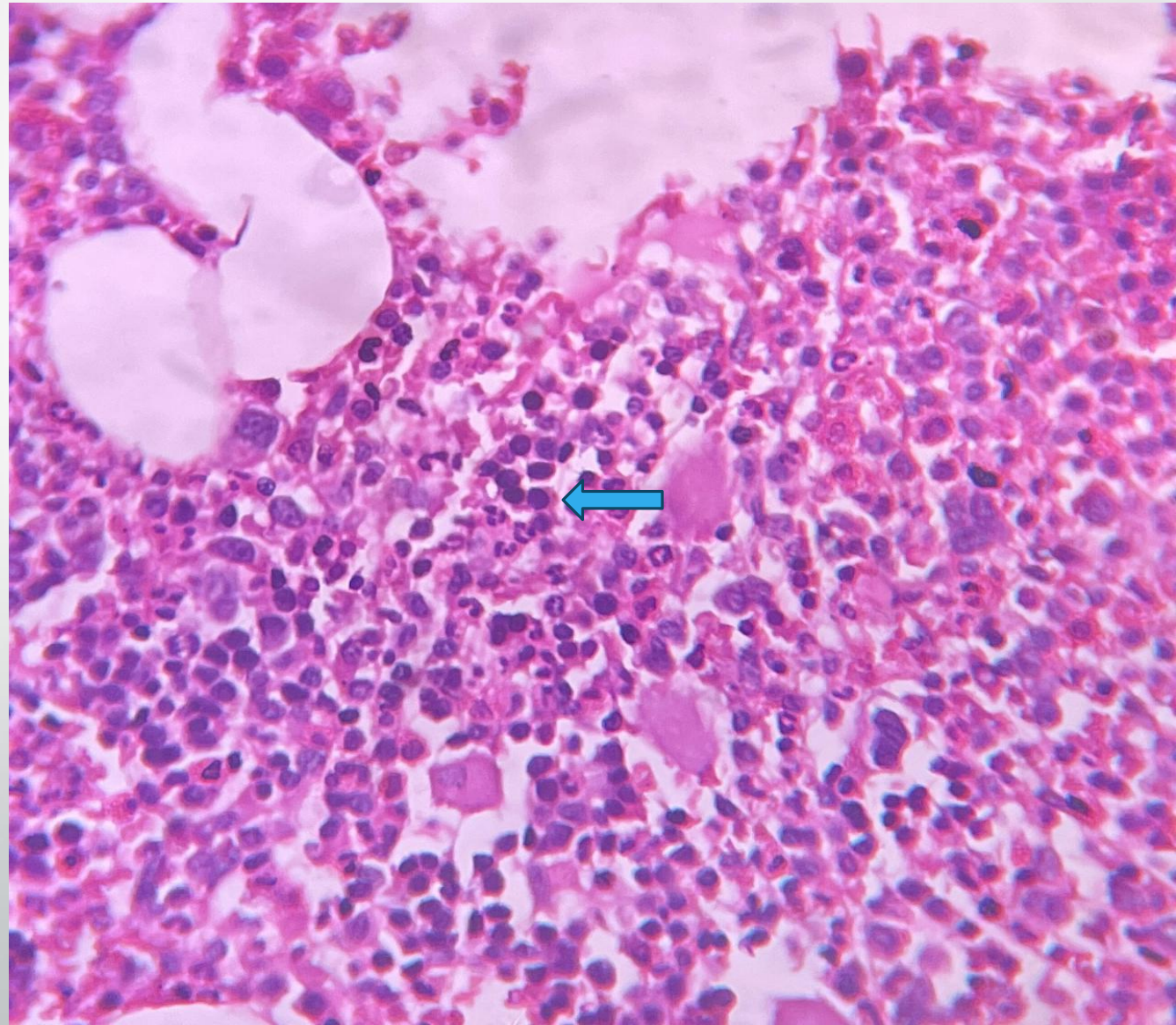
B- Dutcher body (intranuclear inclusion).

C- Flame cell.

BONE MARROW BIOPSY

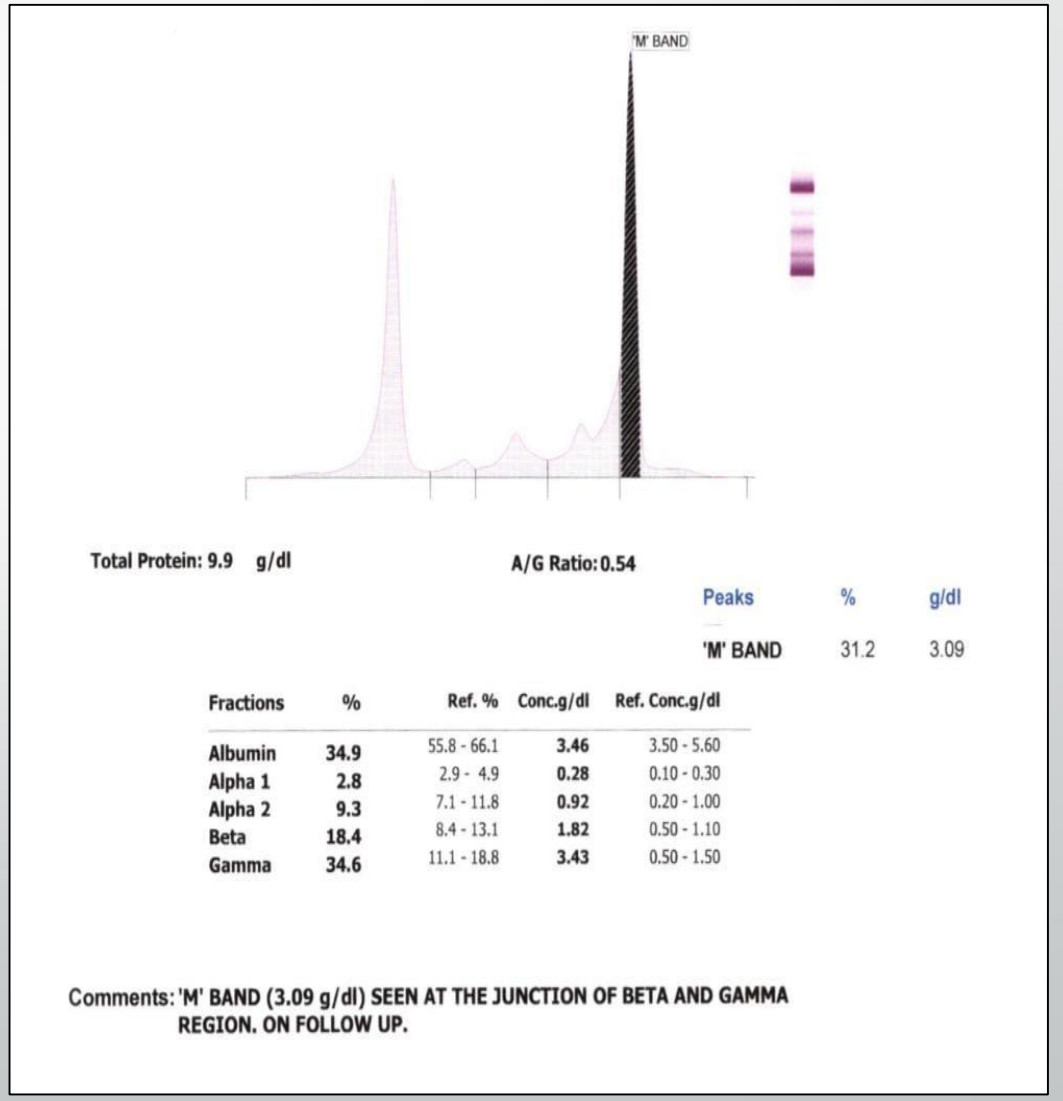
- Hypercellular bone marrow biopsy shows focal clusters of plasma cells.
- Immunohistochemistry on bone marrow biopsy–

  CD138 highlights 25% plasma cells.
- The plasma cells are Lambda chain restricted and immuno-negative for CD20.



SERUM PROTEIN ELECTROPHORESIS TEST

M band (3.09 g/dl) seen at the junction of beta and gamma region.



SERUM PROTEIN ELECTROPHORESIS WITH IMMUNOFIXATION

- Immunofixation Electrophoresis – Monoclonal Gammopathy seen in IgM and Lambda region.

SERUM FREE LIGHT CHAIN ASSAY

- Free light chain assay Lambda restricted plasma cells.

Immunofixation Electrophoresis - Qualitative, Serum

Immunoglobulins	Observed Band	Biological Reference Interval
IgG	**Absent**	Absent
IgA	**Absent**	Absent
IgM	**Present**	Absent
Kappa	**Absent**	Absent
Lambda	**Present**	Absent
M-Band	**Present**	Absent

COMMENT : MONOCLONAL GAMMOPATHY SEEN IN IgM AND LAMBDA REGION.
.ON FOLLOW UP.

Test Description	Observed Value	Biological Reference Interval
Free Kappa (Light Chain),Serum by Nephelometry	**6.48**	3.30 to 19.4 mg/L
Free Lambda (Light Chain),Serumby Nephelometry	**56.30**	5.71 to 26.30 mg/L
Free Kappa/Free Lambda Ratio, Serum	**0.12**	0.26 to 1.65 In cases with renal impairment suggested referene interval : 0.37 to 3.10 Ref: Hutchison et al, BMC Nephrology 2008

Kindly correlate clinically and follow up.

Interpretation :

1. Serum free light chain (FLC) assays are used for the diagnosis of monoclonal gammopathies along with serum protein electrophoresis (SPE) and immunofixation electrophoresis (IFE).
2. Serial measurement of serum FLC is recommended for monitoring treatment response of monoclonal gammopathies. It may also be used as a prognostic marker.
3. Increased production of monoclonal immunoglobulins or free monoclonal light chains leads to a change in the Kappa/Lambda light chain ratio. A Kappa/Lambda ratio outside the reference interval indicates a possibility of monoclonal gammopathy. In such cases, serum and/or 24hrs urine immunofixation electrophoresis to be considered.
4. Elevated Kappa and Lambda free light chains may occur due to hypergammaglobulinemia or impaired renal clearance.

DIAGNOSIS IS

“IgM MULTIPLE MYELOMA”

WHO 2021 Classification Diagnostic Criteria for Multiple Myeloma

- **Multiple myeloma**

Essential:

Clonal bone marrow plasma cells ≥ 10% or biopsy-proven bony or extramedullary plasmacytoma.

AND

- Any one or more of the following myeloma-defining events:

Evidence of end-organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:

- Hypercalcaemia: serum calcium > 0.25 mmol/L (> 1 mg/dL) higher than the upper limit of normal or >2.75 mmol/L (>11mg/dL)
- Renal insufficiency: creatinine clearance < 40 mL per minute or serum creatinine > 177 μmol/L (> 2 mg/dL)
- Anaemia: haemoglobin value > 2 g/dL below the lower limit of normal, or a haemoglobin value of < 10 g/Dl
- Bone lesions: one or more osteolytic lesions on skeletal radiography, CT, or PET-CT

OR

Clonal bone marrow plasma cell percentage ≥ 60%

OR

Involved: uninvolved serum free light chain ratio ≥ 100 (involved free light chain level must be ≥ 100 mg/L)

OR

More than one focal lesion (≥ 5 mm in size) on MRI studies

IgM vs IgG Multiple Myeloma

- IgM Myeloma:

1. Accounts for 1-2% of MM cases

2. Typically associated with:

- Older age - Female predominance

- Lower serum albumin

- Higher serum lactate dehydrogenase (LDH)

3. Often presents with:

- Anemia
- Thrombocytopenia
- Hepatosplenomegaly

4. Genetic features:

- More frequent deletions of 13q14
- Less frequent t(4;14) translocations

- IgG Myeloma:

1. Accounts for 50-60% of MM cases

2. Typically associated with:

- Younger age
- Male predominance
- Lower serum LDH

3. Often presents with:

- Bone pain
- Hypercalcemia
- Renal impairment

4. Genetic features:

- More frequent t(4;14) translocations

- Less frequent deletions of 13q14

TAKE HOME MESSAGE

- The number of plasma cells varies from barely increased to > 90% on marrow.
- Rare PCM/MM cases may show < 10% plasma cells in the aspirate smears, likely caused by a suboptimal bone marrow aspirate or focal distribution of disease in the marrow.
- In such instances, trephine biopsy sections may show more plasma cells with or without focal clusters / nodular aggregates or sheets of plasma cells.
- After identifying an M-band on SPEP, subsequent immunofixation electrophoresis is necessary to establish the monoclonal protein's heavy chain and light chain composition.


Thank
you !