CASE OF THE MONTH (APRIL)

Dr Namrata Kaul

Chief complaints

- 79 year old female presented with complaints of evening rise of temperature, significant loss of weight and appetite.
- History of dry skin was present since childhood
- Also symptoms of gastrointestinal discomfort and bony pain were seen.

Examination

- General physical examination

✓ Pallor +

✓ Periorbital erythema +

- Systemic Examination

❑Perabdominal

✓Hepatosplenomegaly +

✓No Lymphadenopathy

❑Respiratory and CVS - NAD

Investigations

- PET SCAN : Hepato-splenomegaly with multiple mild metabolically active abdominal lymphnodes and extensive metabolically active sclerotic lesions in bones. Hypermetabolism was seen in relation to spleen
- GI Endoscopy : Esophagitis and Duodenitis
- Liver function tests and kidney function tests were normal.

Haematological investigation

- **CBC and Peripheral Smear :**

✓ Hb: 10g/dL

✓ Platelet count :>1 lakh/per cu mm on smear

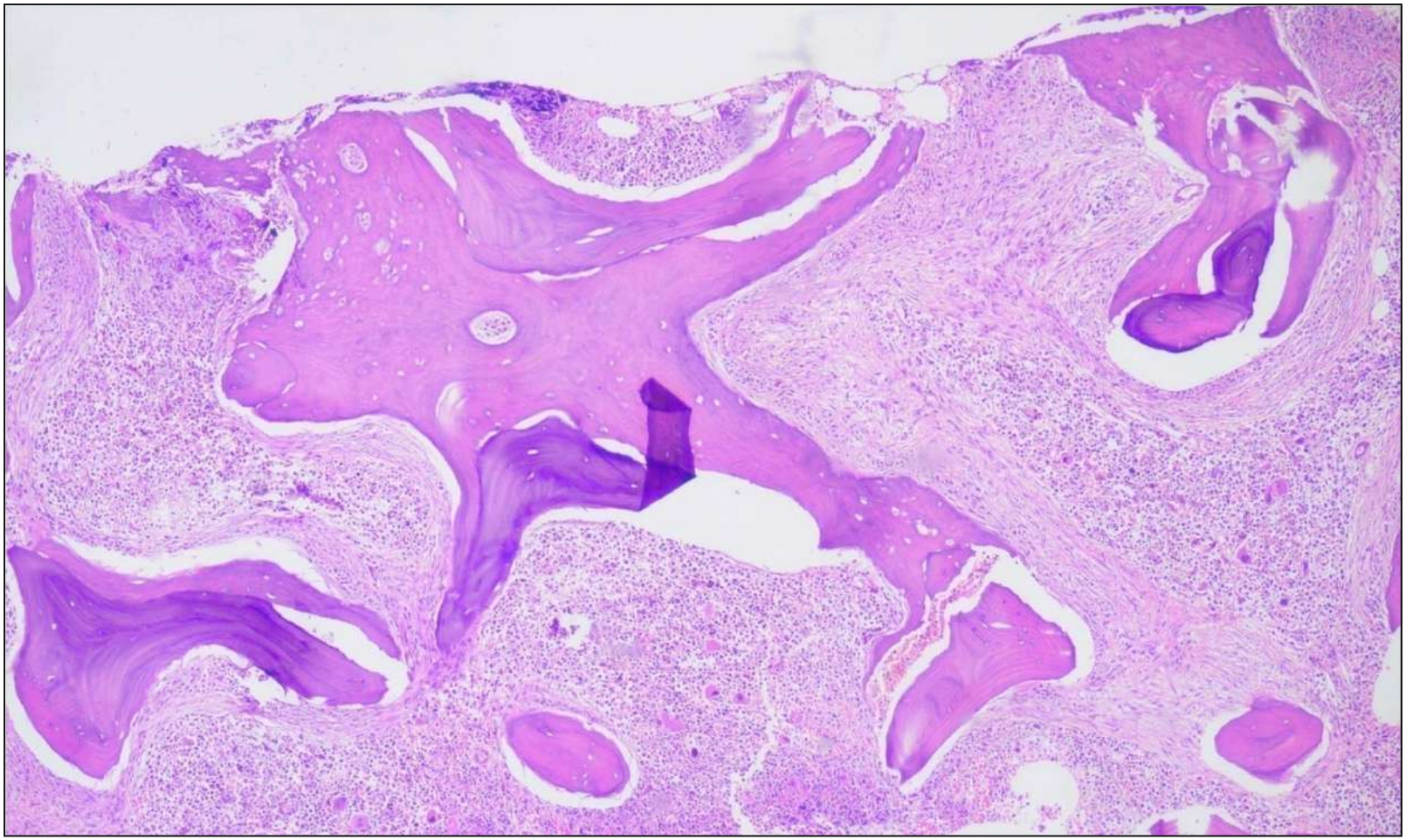
✓ WBC : shows adequate counts with leukoerythroblastic blood picture. No atypical cells seen

- **Bone marrow aspiration:**

  Cellular reactive bone marrow shows all hemopoeitic cells adequately alongwith increased megakaryocytes and many young forms. No atypical cells were seen

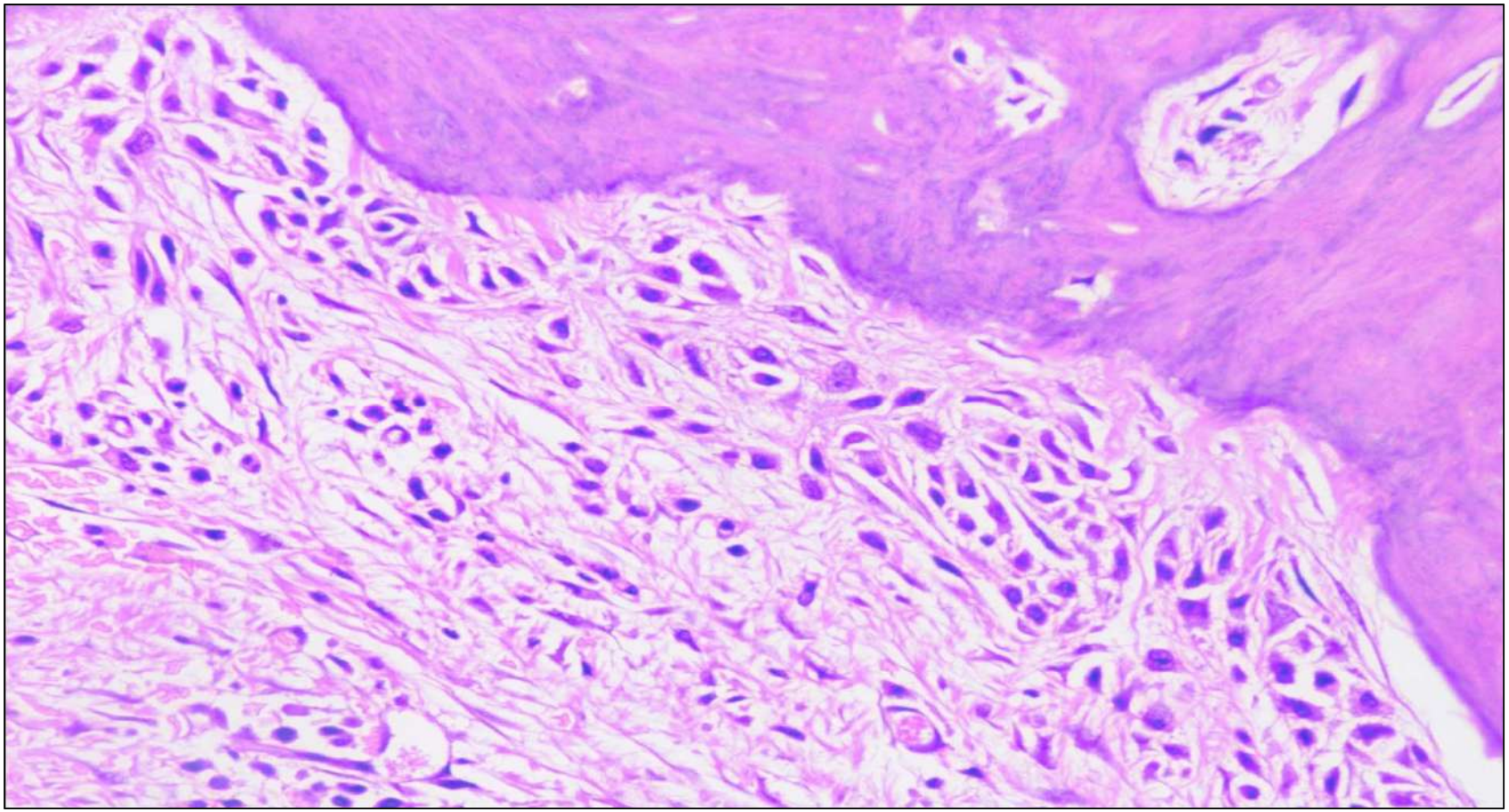
- **Cytogenetics** : Normal female karyotype

Bone marrow biopsy



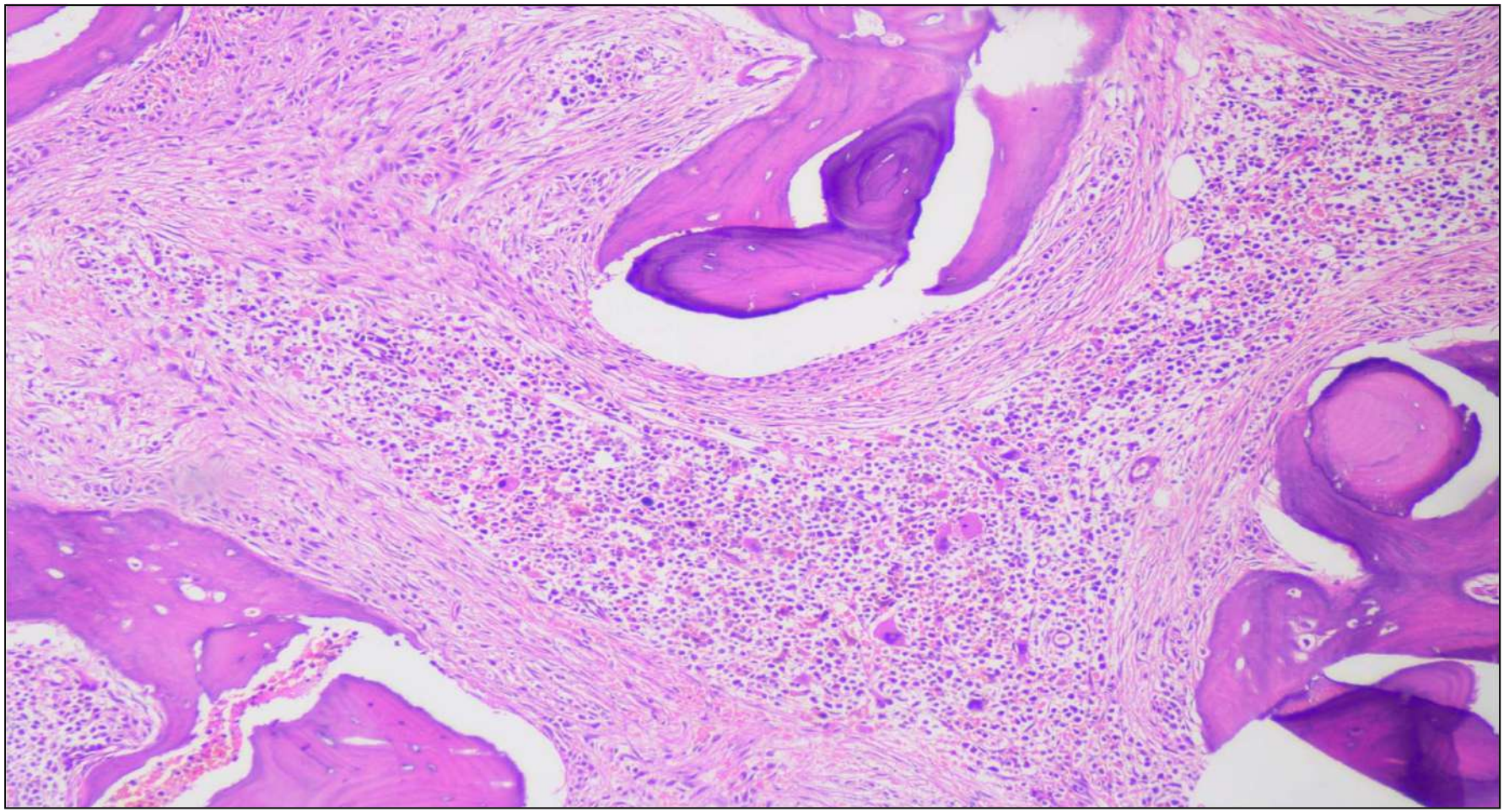
HYPERCELLULAR MARROW SHOWING PARATRABECULARLY ARRANGED ATYPICAL CELLS AND FIBROSIS

Bone marrow biopsy

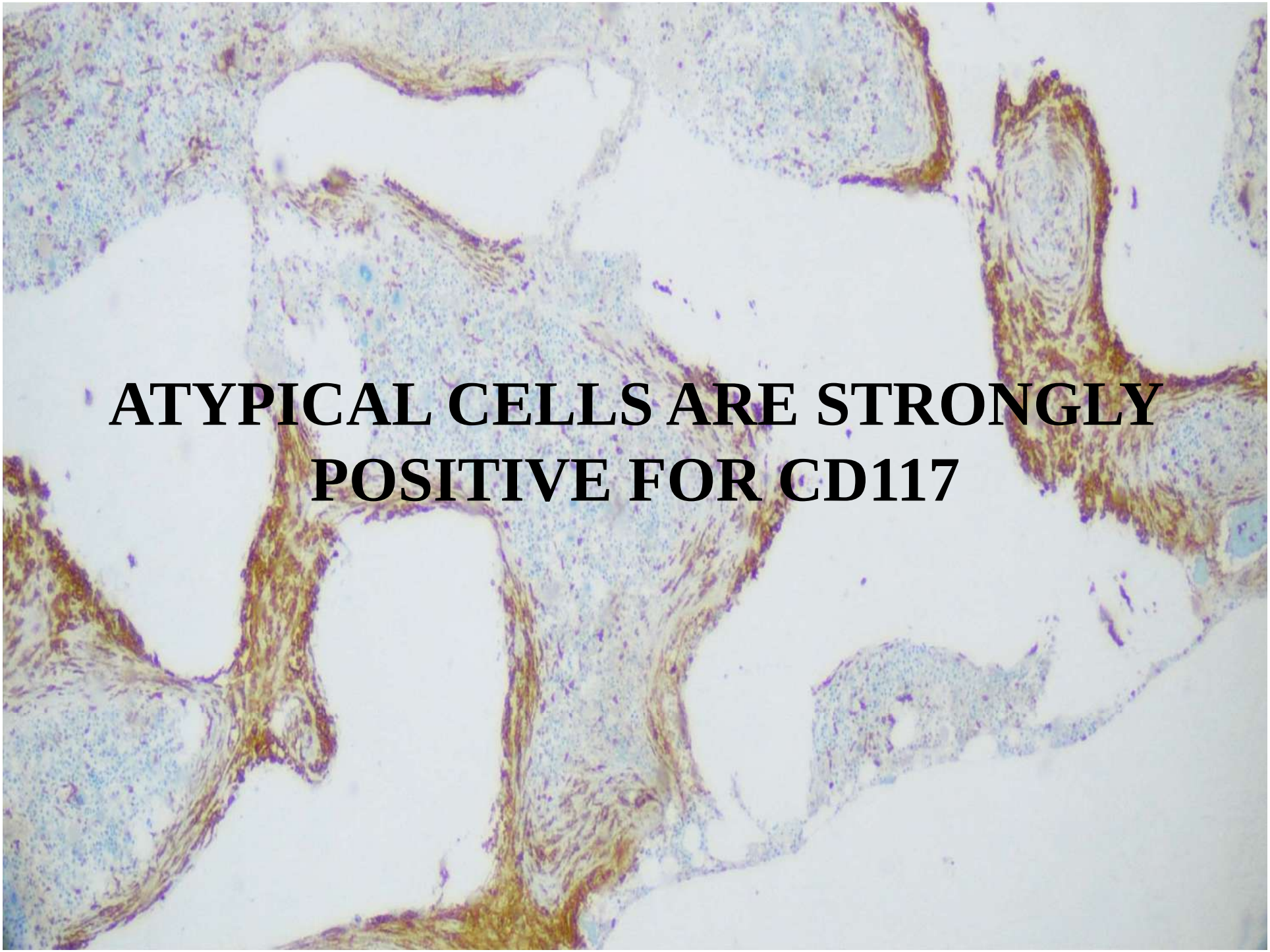


PARATRABECULARLY ARRANGED ATYPICAL CELLS ARE SMALL TO INTERMEDIATE IN SIZE HAVING ROUND TO OVAL TO SPINDLED SHAPED NUCLEUS

Bone marrow biopsy



INCREASED MEGAKARYOCYTES WITH MANY SHOWING NUCLEAR LOBULATION, LOOSE CLUSTERING AND HYPERCHROMATIC NUCLEUS


ATYPICAL CELLS ARE STRONGLY
POSITIVE FOR CD117

Probable Diagnosis

Systemic Mastocytosis with an associated hematological neoplasm(MPN)

On further investigations

- BCR-ABL, CALR, MPL, JAK2 EXON 12 WERE NEGATIVE

Final Diagnosis

Systemic Mastocytosis

Further investigations adviced

- KIT D816V mutation studies
- Serum parathyroid levels (in view of bone change and paratrabecular fibrosis)
- Serum tryptase level

Systemic Mastocytosis

- Mastocytosis occurs due to clonal neoplastic proliferation of mast cells that accumulate in one or more systemic organs
- TYPES :

✓Cutaneous mastocytosis

✓Systemic mastocytosis

Systemic mastocytosis

- Generally diagnosed after 2nd year of life
- Bone marrow is almost always involved

Clinical features

- ✓ Constitutional symptoms : fever, weight loss, fatigue
- ✓ Skin manifestations : Pruritis, urticaria, flushing
- ✓ Mediators related systemic events: GI distress, syncope, headache, hypotension
- ✓ Muskuloskeletal symptoms : Bone pain, Osteopenia, Osteoporosis, Fracture, Myalgia

Diagnostic criteria for systemic mastocytosis

- **Diagnosis can be made with one major and one minor criterion or when >/= 3 minor criterion are present**
- MAJOR CRITERIA: Multifocal dense infiltrates of mast cells(>/= 15 aggregates) detected in bone marrow biopsy/ extracutaneous tissues
- MINOR CRITERIA:

1. In bone marrow biopsy/ extracutaneous tissues, > 25% mast cells in infiltrate have spindle shape/atypical morphology or > 25% mast cells in infiltrate are immature/atypical

Diagnostic criteria for systemic mastocytosis contd…

2. Activating point mutation at codon 816 of KIT in BM/Blood/ extracutaneous tissue
3. Mast cells in BM/Blood/ extracutaneous tissue express CD 25 with or without CD 2 in addition to normal mast cell markers.
4. Serum total tryptase >20ng/dl , unless associated myeloid neoplasm present

Variants of systemic mastocytosis

Indolent systemic mastocytosis

Meets the general criteria for systemic mastocytosis

No C findings[a]
No evidence of an associated haematological neoplasm
Low mast cell burden
Skin lesions are almost invariably present

Bone marrow mastocytosis

As above (indolent systemic mastocytosis), but with bone marrow involvement and no skin lesions

Smouldering systemic mastocytosis

Meets the general criteria for systemic mastocytosis

≥2 B findings; no C findings[a]
No evidence of an associated haematological neoplasm
High mast cell burden
Does not meet the criteria for mast cell leukaemia

Systemic mastocytosis with an associated haematological neoplasm

Meets the general criteria for systemic mastocytosis
Meets the criteria for an associated haematological neoplasm (i.e. a myelodysplastic syndrome, myeloproliferative neoplasm, acute myeloid leukaemia, lymphoma or another haematological neoplasm classified as a distinct entity in the WHO classification)

Aggressive systemic mastocytosis

Meets the general criteria for systemic mastocytosis

≥1 C finding[a]
Does not meet the criteria for mast cell leukaemia
Skin lesions are usually absent.

Mast cell leukaemia

Meets the general criteria for systemic mastocytosis

Bone marrow biopsy shows diffuse infiltration (usually dense) by atypical, immature mast cells.
Bone marrow aspirate smears show ≥20% mast cells.
In classic cases, mast cells account for ≥10% of the peripheral blood white blood cells, but the aleukaemic variant (in which mast cells account for <10%) is more common.
Skin lesions are usually absent.