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Tetranucleated Plasmocyte and Multiple Myeloma: Concerning A Case

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Abstract | **Case Report**

A tetranucleated plasma cell in a blood smear is a morphological anomaly that suggests a pathological context, often associated with malignant proliferations (notably multiple myeloma). We report the case of a patient being monitored for severe evolving multiple myeloma, and we present through this work the morphological changes of plasma cells in this context.

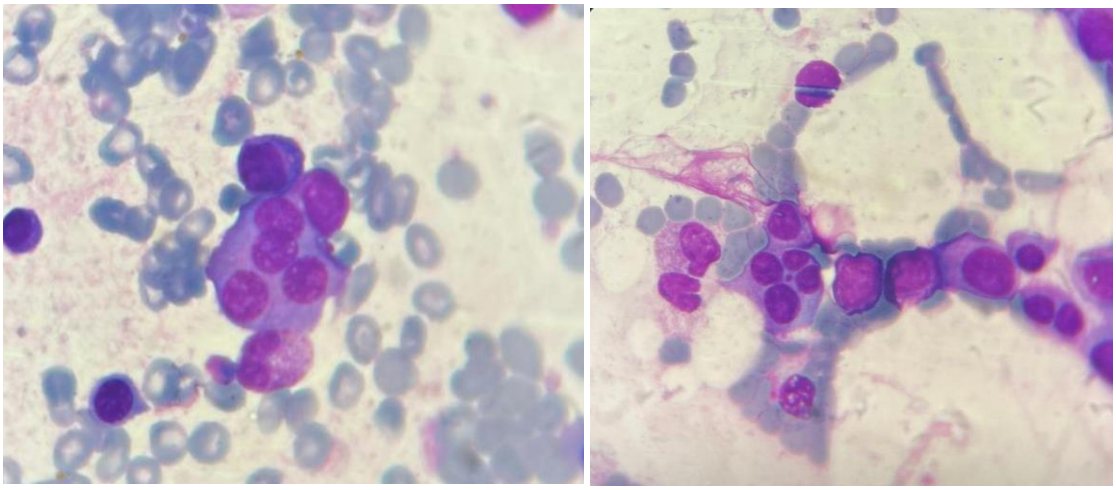
Keywords: Tetranucleated plasmocyte - multiple myeloma - Hematology.

INTRODUCTION

A tetranucleated plasmocyte is a marker of severe atypia, highly suggestive of a malignant plasma cell disorder (particularly multiple myeloma). Its identification requires rigorous verification of morphology (cytology/histology), with additional investigations in hematology (molecular biology, imaging), and clinical correlation (symptoms, biological assessment). Recognizing this entity is important to avoid any diagnostic confusion.

OBSERVATION

We report the case of a 71-year-old patient, followed for severe multiple myeloma, admitted to the emergency department for a pathological fracture, with no other particular medical history, in whom biological assessment objectively reveals a normochromic normocytic arregenerative anemia with thrombocytopenia. The blood smear shows the presence of abnormal tetranucleated plasma cells, with abundant basophilic cytoplasm and clear perinuclear zones (Figure).



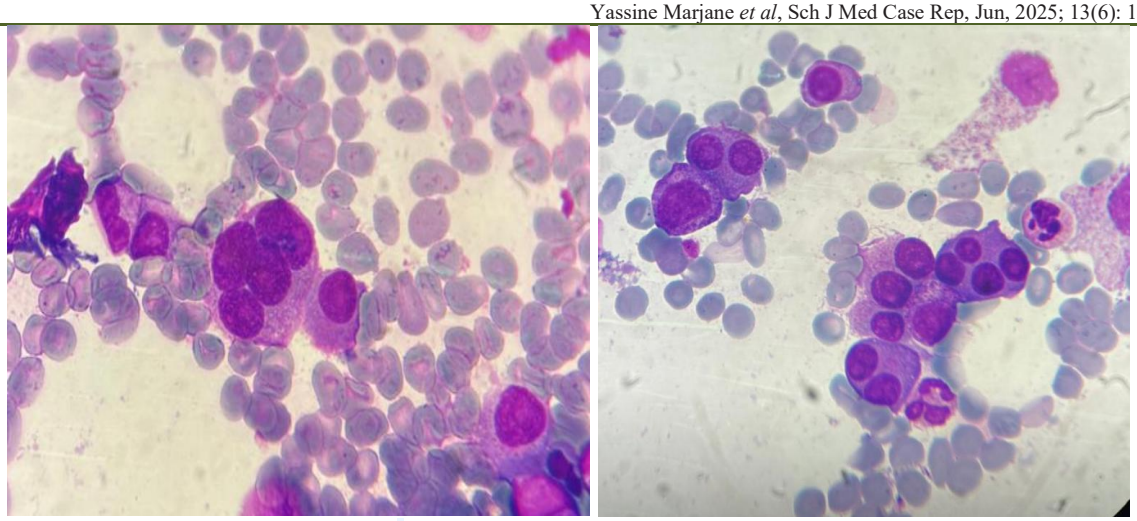


Figure: Abnormal tetranucleated plasma cell

DISCUSSION

The observation of a plasma cell presenting 4 nuclei is a significant morphological anomaly, as normal mature plasma cells are always mononucleated (with a single nucleus). This characteristic suggests a pathological context, often associated with malignant proliferations [1, 2].

The normal plasma cell has a unique eccentrically located nucleus, with chromatin in a 'wheel-spoke pattern' (radial arrangement), abundant basophilic cytoplasm (blue-purple in standard stains), and a clear perinuclear zone (developed Golgi apparatus). It varies in size (10-20 µm), but is never multinucleated. A tetranucleated plasma cell is never normal and warrants further investigation.

A tetranucleated plasmocyte (4 nuclei) is a heavily suggestive anomaly of malignant plasmacytic proliferation, primarily in multiple myeloma, characterized by the presence of abnormal plasmocytes ("atypical" or "immature" plasmocytes). The morphological criteria of malignancy include: multiple nuclei, increased size, prominent nucleoli, nuclear asymmetry.

Other pathologies pose differential diagnosis with myeloma [3]:

- Waldenström's lymphoplasmacytic disease.
- AL amyloidosis.
- Exceptionally, in severe chronic inflammatory reactions.

Several possible mechanisms may be the cause of this anomaly:

- Mitotic anomaly: Failure of cytokinesis after nuclear replication (endomitosis), leading to a multinucleated cell.
- Genetic instability: Frequent in malignant clones (e.g., mutations in cell cycle genes).
- Cell fusion: Theoretical, but poorly documented in plasma cells.

Additional tests are necessary to confirm a malignant hematopathy:

- Bone marrow biopsy (analysis of the bone marrow).
- Immunophenotyping (markers: CD138+, CD38+, cytoplasmic restriction of light chains κ/λ).
- Serum protein electrophoresis (search for a monoclonal spike).
- Cytogenetic analysis (search for 17p deletion, translocation t(4;14), etc.).

On the microscopic morphological level of plasma cells, the differential diagnosis is made with certain situations [4, 5]:

- Osteoclast (multinucleated giant cell from the bone marrow, CD68+).
- Megakaryocyte (large polyploid cell, single multilobated nucleus).
- Technical artifact: Superposition of several cells on the smear.

The microscopic aspect of plasma cells in multiple myeloma, observed mainly under the optical microscope on bone marrow smears (myelogram) and bone marrow biopsies:

1. Massive infiltration: The major criterion is the significant increase in the percentage of plasma cells in the bone marrow (usually ≥ 10-15%, often much more). These plasma cells sometimes form clusters or cohesive areas.

2. Pleomorphism (morphological variability):

- Size: Very variable, ranging from small plasma cells resembling lymphocytes to giant plasma cells.
- Shape: Sometimes very irregular (asymmetry).

3. Nuclear anomalies:

- Increased size.
- Chromatin: Loss of the characteristic dense and regular 'wagon wheel' appearance. Chromatin may appear finer, more sparse, or irregular.
- Nucleoli: Often prominent and visible (sometimes multiple), which is rare in normal mature plasma cells. Sign of immaturity or atypia.
- Pluricentricity: Frequent presence of binucleated or multinucleated plasma cells that sometimes resemble giant cells (as in our case).

4. Cytoplasmic anomalies:

- Inclusions: Consequence of excessive production and poor "packaging" of monoclonal immunoglobulins.
- Russell bodies (or Russell droplets): Spherical inclusions, red or pink (in HE or MGG), corresponding to aggregates of immunoglobulins in the endoplasmic reticulum.
- Flame cells: Diffuse reddish/pink cytoplasm (MGG) due to a diffuse accumulation of glycoproteins (often IgA).
- Mott cells: Plasma cells containing numerous clear vacuoles (corresponding to Russell bodies dissolved during preparation).
- Crystals: Intracytoplasmic (or sometimes intranuclear) crystalline inclusions, very characteristic but not very common.
- Dutcher inclusions: PAS-positive intranuclear inclusions, corresponding to invaginations of the cytoplasm containing immunoglobulins.
- Vacuolization: Cytoplasm containing clear vacuoles of variable size.
- Color: Basophilia (blue color in MGG) can be very intense or, on the contrary, paler and grayish.

5. Differentiation and aggressiveness: The most mature forms resemble normal plasma cells but are in excessive numbers. The immature forms have a more central nucleus, finer chromatin, prominent nucleoli, and a higher nucleocytoplasmic ratio. Pleomorphic or anaplastic forms show major atypia (very large cells, multiple and irregular nuclei). These forms are often associated with a more aggressive disease.

Other microscopic techniques can be useful for diagnosis. Histology (Bone marrow biopsy): Confirms infiltration (often nodular or diffuse), atrophy of normal hematopoiesis, and associated osteolysis. Immunohistochemistry (CD138, CD56, Ki67, kappa/lambda light chains) is crucial to confirm clonality and assess proliferation. Flow cytometry: Allows for the precise detection of the clonal plasma cell population (abnormal expression of CD19-, CD56+, CD117+, restricted light chains) even if it is minority or of little atypical morphology [1, 6].

Microscopic study is of vital clinical importance [2, 4, 6]:

- Morphology aids in diagnosis (abnormal plasma cell infiltration).
- It provides clues about the aggressiveness of the disease (immature/pleomorphic forms often have a poorer prognosis).
- It guides additional tests (immunophenotyping, molecular biology).

CONCLUSION

The plasmocytes of multiple myeloma are microscopically characterized by their increased number and marked pleomorphism, with frequent nuclear abnormalities (size, chromatin, nucleoli, multinucleation) and cytoplasmic abnormalities (various inclusions, vacuolization). These atypical features reflect the malignant nature and the aberrant production of immunoglobulin by the plasmacytic clone.

Conflict of Interest: The authors declare that they have no conflict of interest.

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