Multiple myeloma – laboratory aspects

Mieloma múltiplo - aspectos laboratoriais

Nydia Strachman Bacal¹, Mariana Ferreira de Assis Funari²

Multiple myeloma (MM) corresponds to 10% of hematological neoplasms and represents 1% of all deaths in the Western hemisphere(1). The diagnostic criteria are bone marrow plasmocytosis (figures 1 and 2), presence of serum monoclonal gammapathy, urine Bence Jones protein and osteolytic lesions (figure 3), especially of punched-out appearance in the skull(2).

Durie(3) proposed the following as major criteria: 30% of plasma cells in the bone marrow, serum IgG concentration of 3.5 g/dl, IgA of 2.0 g/dl and a kappa or lambda light chain of 1.0 g/24h in the urine. The minor criteria included bone marrow plasma cells between 10 and 30%, serum immunoglobulins or urinary quantification of light chains less than the reference values above mentioned, lytic bone lesions and suppression of other immunoglobulins. The system requires one major criterion and a minor criterion or three minor criteria in order to confirm the diagnosis of MM.

Bone pain, mainly in the spine, as well as spontaneous pathological fractures are the major symptoms of the disease (figure 3). When osteolytic lesions are present in X-rays, electrophoresis should be performed to investigate monoclonal gammapathy. Immunofixation is considered the gold standard method for identifying this monoclonal component (figure 4). Renal failure is one of the major complications of MM.

¹ Hematologist and Clinical Pathologist of the Clinical Pathology Department Hospital Israelita Albert Einstein - São Paulo (SP) – Brazil.
² Biomedical Scientist. Graduate Course in Laboratory Hematology by the Department of Clinical Pathology Hospital Israelita Albert Einstein - São Paulo (SP) – Brazil.

Corresponding author

Received on April 4, 2005 – Accepted on May 9, 2005
Patients with MM frequently present with normocytic and normochromic anemia with high erythrocyte sedimentation rate. The Rouleaux Formation may be identified in peripheral blood smears and corresponds to a piling of red blood cells resulting from alterations in electrical charges due to the interference of anomalous serum immunoglobulin.

The immunophenotypic study helps to identify anomalous plasma cells. The demonstration of monoclonal intracytoplasmic immunoglobulins confirms the diagnosis of MM, and helps to make the differential diagnosis with other types of plasma cell dyscrasias.

Normal plasma cells generally express CD45, CD38, CD138 surface antigens and polyclonal intracytoplasmic immunoglobulins. Myeloma cells present similar phenotype. They usually express CD38 and CD138 but, in most cases, the cells express CD56, which is a typical NK cell marker, related to cell adhesion. CD45 generally presents low or absent expression. CD117, a mark of immaturity, may be present. Immunoglobulin expression is intracytoplasmic and monoclonal. Thus, in the CD138 positive population, the strong expression of CD38, weak or absent expression of CD45 concomitant to CD56 indicate malignancy (figure 5).

The utilization of immunophenotyping is more than identifying neoplastic cells. The presence of residual disease after treatment can be sought through aberrant phenotypes or asynchronisms detected at diagnosis. The weak expression of CD38 and CD45, which can be even negative, in addition to the expression of CD19, CD20, CD28, CD33 and of surface immunoglobulins can be used for this purpose.

Another application of flow cytometry is the kinetic study of the DNA cycle that assesses the proliferation rate of neoplastic cells and can be used as a prognostic factor. Flow cytometry allows the evaluation of ploidy of anomalous cells and also enables the analysis of the amount of cells in the cellular cycle synthesis phase (S). Both the presence of aneuploidy and the amount of S phase cells have prognostic implications (figure 6).
Cytogenetic analysis is essential as a prognostic value. G band analysis and fluorescence *in situ* hybridization (FISH) can be carried out and show both numerical and structural changes.

The most common structural abnormality is translocation of 14q32, the deletion or loss of 13q, and deletion of 17q(4).

**References**