Introduction

Plasma cells are formed by B-lymphocytes and produce specific antibodies against pathogens. They therefore play a central role in the humoral immune response. Abnormalities (clonal expansion) of plasma cells leads to the formation of atypical immunoglobulins (clonal immunoglobulins/paraproteins) by the cells, which do not benefit the infectious response; they can be detected in serum and urine. Several different clinical presentations of disease are assigned to plasma cell neoplasias: Solitary plasmacytoma, multiple myeloma (MM), plasma cell leukemia and a monoclonal gammopathy of undetermined significance (MGUS).

Detection of clonal immunoglobulins (paraproteins)

An increased proportion of the immunoglobulins can be detected by protein electrophoresis. There, the picture of a M-gradient is seen. By means of immune fixation, the clonal origin of the proteins can be detected and further clarified which immune globulin type is increased (e.g. IgG, IgA, IgD, IgE etc.). The determination of the paraprotein concentration is also performed in the context of follow-up controls. In most cases, the concentration correlates with the disease activity (high concentration = high disease activity, low concentration = low disease activity).

Solitary plasmacytoma

This is a discreet (isolated) tumor composed of plasma cells. It can occur inside or outside of the bone/bone marrow (intraosseous or extramedullary). The formation of small amounts of clonal immunoglobulins results.

Multiple myeloma (MM)

Multiple myeloma is a clonal plasma cell proliferation in the bone marrow. The cells produce a clonal immunoglobulin (paraprotein), which can be detected in the serum or urine. An M-gradient can be detected by serum protein electrophoresis and the paraprotein Ig-type determined in the further immunofixation (in approx. 60% of cases they are IgG, in 20% IgA and very rarely IgD or IgE). Bence Jones-proteins appear in the urine. Bone lesions (osteolytic nodes) can be found in some of the patients by imaging procedures. They result from the release of osteoclast-activating substances from the abnormal plasma cells. The resultant osteolysis can lead to a strong increase in the serum calcium level.

Over the course of the disease, renal injury is often caused by paraproteins and hypercalcemia. Increasing anemia develops (replacement process in the bone marrow and lacking stimulation by erythropoietin from the damaged kidneys). Occasionally, thrombocytopenia also develops. Multiple myeloma is responsible for approx. 15% of all malignant hematological diseases. The occurrence is increased in people 50 years of age and above. Men are affected more frequently than women.

Plasma cell leukemia

In plasma cell leukemia, the plasma cell proportion of leukocytes in the peripheral blood exceeds 20% or 2.0 g/L. Plasma cell leukemia can appear both primary, as the first disease, and secondary as a progression step with multiple myeloma.

Monoclonal gammopathy of undetermined significance (MGUS).

One speaks of MGUS when clonal immunoglobulins are detected in the serum (< 30 g/L) without other changes, such as those found with multiple myeloma (no osteolysis, no hypercalcemia, no kidney damage, no anemia). The plasma cell proportion in the bone marrow must be less than 10% and lymphoproliferation arising from the B-cell type must be ruled out. Multiple myeloma may develop from MGUS over the further course.

Bone Changes

In multiple myeloma, bone lesions are typically found that can be seen by imaging techniques (X-ray, CT, etc.). The lesions include osteolytic nodes (localized zones of dissolved bone) or also a diffuse bone substance reduction (osteoporosis). These lead to rheumatic and similar complaints in the patient and to pathological fractures. These early symptoms often bring the patient to the doctor. Pain therapy or physical therapy is often prescribed to relieve the discomfort. Multiple myeloma is often diagnosed only when other symptoms appear, such as anemia, susceptibility to infections, renal impairment or hypercalcemia.

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Normal plasma cells

Normal plasma cells can usually be easily identified. They are medium in size, round to oval, with medium-wide to wide, mostly dark-basophilic cytoplasm, which is usually clearly brighter around the nucleus (perinuclear halo). The nucleus is eccentrically located with dense, lumpy nuclear chromatin.

Plasma cells in multiple myeloma / plasma cell leukemia

Plasma cells that are washed out with multiple myeloma and plasma cell leukemia often show atypical morphologies ("myeloma cells"). These include:

- nuclear chromatin dense and loose (blast-like)
- isolated prominent nucleoli (nuclear bodies)
- binuclear or polymorph nuclear forms
- bright cytoplasm color
- no perinuclear brightening of the cytoplasm
- asynchrony: different maturity stage of nucleus and cytoplasm
- nuclei no longer eccentrically located

Rouleaux formation and protein film

Rouleaux formation

Due to their negative surface tension (zeta-potential), erythrocytes normally repel each other so that a minimum distance of approx. 25 nanometers between the cells is created. Because of the increased presence of plasma proteins, this zeta potential is reduced. The erythrocytes move closer together and aggregate to formations resembling stacked coins.

Protein film

Plasma with a high protein content assumes a light purple hue (protein film, plasma layer) in bloodstains. Isolated fine lines also appear.