

# Multiple myeloma

EBMG  
27.12.2001

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## Aim

- Early diagnosis is important, especially in order to prevent irreversible kidney lesions.

## Pathology

- MM is a clonal haematopoietic malignancy in which malignant plasma cells accumulate in the bone marrow and produce an immunoglobulin, usually monoclonal IgG or IgA (an M component).
- Common complications include recurrent bacterial infections, anaemia, osteolytic lesions, and renal insufficiency.
- MGUS (monoclonal gammopathy with undetermined significance) is marked by the presence in the serum of monoclonal IgG or IgA without evidence of MM. Some of these patients (as many as 16% during a 30-year or longer follow-up period) develop MM. It is evident, however, that this outcome is less frequent among healthy individuals with an M component, the condition preferentially called benign paraproteinaemia. Only < 1% of these subjects develop MM.

- Approximately 2 - 3 new cases/100,000/year.
- Diagnosis is usually made at the age of 50 - 70 years; rarely under the age of 40 years.
- No sex differences.

## Aetiology

- In individual patients it remains unknown.
- Ionising irradiation slightly increases the risk.

## Diagnosis

- The main diagnostic difficulty is to make a distinction between early cases of MM and non-myeloma paraproteinaemias, especially MGUS.
- The diagnosis of MM depends on finding:
  - marrow infiltration by plasma cells (> 30%)
  - lytic bone lesions
  - monoclonal protein in serum (> 35 g/L IgG; > 20 g/L IgA) and/or urine (> 1 g/24 hours).

## Differential diagnostics

- In most cases of MGUS:
  - No symptoms and signs
  - No lytic bone lesions
  - Bone marrow plasmacytosis < 10%
  - M component smaller than in MM; IgG < 30 g/L, IgA < 10 g/L, urine protein < 1 g/24 hours
  - Polyclonal immunoglobulins normal
- Waldenström's macroglobulinaemia (See related EBM Guideline: **Waldenström's macroglobulinaemia** available on the EBM Web site)
- Lymphomas with an M component
- Other rare diseases where there is an M component

## Clinical picture

- Often:
  - Osteolytic lesions and bone pains
  - Mild-to-moderate anaemia, hypercalcaemia, hyperuricaemia
  - Renal insufficiency
- Rarely:
  - Hyperviscosity syndrome (IgA myeloma)

## Typical laboratory findings

- Increased erythrocyte sedimentation rate (not in light-chain myeloma)
- M component in serum and/or urine
- Decreased haemoglobin level, often also leuco- and thrombocytopenia
- Malignant plasma cell infiltrates in the bone marrow
- Osteolytic lesion in bone X-ray (magnetic imaging may be more sensitive)
- Often increased serum urate and calcium but diminished albumin concentration

## Basic examinations

- Bone marrow examination
- Serum and urine protein electrophoresis (M component can be found in urine in only 10 - 20% of MM patients)

## Additional investigations when MM is likely

- X-ray (skull, thorax/ribs, backbone, scapulae, pelvis and long bones of the extremities)
- Serum/plasma total protein, albumin, potassium, sodium, calcium, ionised calcium, creatinine, urate and immunoglobulins (IgG, IgA, IgM)
- Identification of M component heavy and light chains by immunofixation or by other means

## Complications

- Renal insufficiency
- Pathological bone fractures
- Hypercalcaemia
- Hyperviscosity syndrome rarely (mostly in IgA myeloma)
- Amyloidosis as a late complication
- Sometimes plasma cell leukaemia, myelodysplastic syndrome or acute leukaemia

## Disease progression and prognosis

- Median life expectancy at diagnosis is about 3.5 - 4 years. Marked individual variation exists.
- Myeloma cell infiltrates occupy the bone marrow causing anaemia as well as leuco- and thrombocytopenia.
- Myeloma cells become gradually resistant to chemotherapy.
- Infections, haemorrhages and renal insufficiency are frequent complications.

## Follow-up and treatment

- If the patient is symptomless, no chemotherapy will be given.
- Treatment is given actively to relieve symptoms.

**In follow-up, attention is paid to**

- The amount of M component (serum and/or urine)
- General condition and symptoms, infections and (bone) pains
- Osteolytic lesions (X-ray)
- Renal function, hypercalcaemia and blood picture.

## Supportive therapy includes

- Maintenance of fluid and electrolyte balance
- Treatment of hypercalcaemia
- Treatment of infections
- Maintenance of mobility in order to prevent osteoporosis and pathological fractures
- Bisphosphonates (to treat hypercalcaemia and to prevent fractures) (Level of Evidence = A; Evidence Summary available on the EBM Web site)

## Chemotherapy

- According to instructions given by a specialist
- Melphalan (cyclophosphamide) and predniso(lo)ne are used for the initial therapy
- Refractory cases
  - VAD (vincristine, doxorubicin, and dexamethasone) or similar combinations
  - High-dose melphalan
- Interferon may be tried, but benefit is uncertain (Level of Evidence = B; Evidence Summary available on the EBM Web site)

## High-dose therapy and stem cell transplantation

- Autologous transplantation is considered for most patients (who appear to tolerate high-dose chemotherapy) under the age of 65 - 70 years (Level of Evidence = C; Evidence Summary available on the EBM Web site)
- Rarely, allogeneic stem cell transplantation.

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Article ID: P15031 (015.046)

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