PARAPRTEINAEMIA and MULTIPLE MYELOMA

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Paraproteinaemias

- A gammopathy refers to over-production of one or more classes of immunoglobulin.
- Polyclonal-associated with acute or chronic inflammation such as infection or sarcoidosis, autoimmune disorders or some malignancy.
- Monoclonal-(M-proteins) or monoclonal gammopathies occur as
- a feature of myeloma, lymphoma, amyloidosis, in connective tissue disease e.g. RH.A, or polymyalgia rheumatica, infection, e.g. HIV, in solid tumours and with no underlying cause.
- Gammopathies are detected by immunoelectrophoresis.
Monoclonal gammopathy of uncertain significance, MGUS

• A paraprotein is present in the blood but there are no other features of myeloma, Waldenstrom macroglobulinaemia, lymphoma or related disease, no associated immune paresis or bone lytic lesion, and bone marrow has less than 10% plasma cells. It is associated with age.

• One quarter progress to myeloma or related disorders over 20 years, and measurement of abnormal ratio of kappa to lambda light chain increase the risk of progression, accordingly molecular progression is needed annually in abnormal ratio.
Waldenstrom macroglobulinaemia

• This is a low grade lymphoplasmacytic lymphoma associated with an IgM paraprotein causing hyperviscosity syndrome. It is rare tumour of the elderly males.

• Presentation:
  • Hyperviscosity- nosebleeds, bruising, visual disturbances and delirium.
  • Anaemia, systemic disturbances, splenomegaly and lymphadenopathy.
  • Asymptomatic with IgM paraprotein found on routine screening
  • associated with a raised plasma viscosity.
  • Bone marrow has a characteristic appearance with lymphoid cells, plasma cells and sometimes prominent mast cells.
Management

• In hyperviscosity and anaemia plasmapheresis is required to remove IgM and make blood transfusion possible.

• Chemotherapy with alkylating agent such as chlorambucil has been the main stay of treatment, and controlling disease in over 50% of patients. Fludarabine, Rituximab.
Multiple myeloma

• Multiple proliferation of plasma cells.
• Normal plasma cells are derived from B cells and produce immunoglobulin that contain heavy and light chains, polyclonal.
• In myeloma plasma cells produce immunoglobulin of a single heavy and light chain a monoclonal protein commonly referred to as a paraprotein. In most cases an excess of light chain is produced, and in some cases only light chain is produced which appears in the urine as Bence Jone’s protein, IgG 55%, IgA 21%. Light chain only 22%.
• A few number of plasma cells is present in the circulation, but the majority is present in the bone marrow. These malignant plasma cells produce cytokines, which stimulate osteoclasts and result in net bone absorption resulting in lytic bone lesions causing bone pain, fractures and hypercalcaemia. Marrow involvement can result in anaemia and pancytopenia
Serum Protein Electrophoresis

- Normal
- Multiple myeloma
Clinical features

- Incidence 4/100000, age 60-70 years, Afro-Caribbeans.
- Diagnosis:
  - Increased malignant plasma cells in the bone marrow 10%
  - Serum and or urinary M protein.
  - Skeletal lytic lesion.
  - Bone marrow aspirate, plasma and urine electrophoresis, and skeletal survey are required.
- High ESR over 100ml/hr in multiple occasions is none specific, only 5% have myeloma.
Clinical and laboratory features of multiple myeloma. (ESR = erythrocyte sedimentation rate; NSAIDs = non-steroidal anti-inflammatory drugs.)

**Hyperviscosity**
- Retinal bleeds
- Bruising
- Heart failure
- Cerebral ischaemia

**Abnormal blood tests**
- Anaemia
- Normo- or macrocytic
- Pancytopenia
- Raised ESR
- Hypercalcaemia
- Renal impairment
- Paraproteinaemia
- Immune paresis

**Bone marrow**
- Plasmacytosis > 10%

**Bence Jones proteinuria**
- Serum free light chains

**Amyloid**
- ‘Panda’ eyes
- Nephrotic syndrome
- Carpal tunnel syndrome

**Bone pain/fracture**

**Lytic lesions**
- Lytic lesion eroding right superior pubic ramus and acetabulum
- Lytic lesions in skull

**Renal failure due to:**
- Paraprotein deposition
- Hypercalcaemia
- Infection
- NSAIDs
- Amyloid

**Spinal cord compression**
- Bony collapse
- Extravascular mass

**Fig 23.31** Clinical and laboratory features of multiple myeloma. (ESR = erythrocyte sedimentation rate; NSAIDs = non-steroidal anti-inflammatory drugs.)
Treatment

- Asymptomatic patients with no end organ damage to kidneys, bone or bone marrow treatment may not be required. The so called a symptomatic myeloma and should be monitored closely.
- High fluid intake, for renal impairment and hypercalcaemia.
- Analgesia for bone pain.
- Bisphosphonates for hypercalcaemia and skeletal related events.
- Allopurinol to prevent urate nephropathy.
- Plasmapheresis, if necessary for hyperviscosity.
- Chemotherapy with or without HSCT.
- Thalidomide, alkylating agent Melphalan and prednisolone. MPT.
- If not illegible for transplant and intolerant or unsuitable for thalidomide,
  - Lenalidomide is approved. In younger fitter patients cyclophosphamide, thalidomide and dexamethasone CTD followed by HSCT will improve quality of life, improve survival but doesn’t cure myeloma
- Radiotherapy for localised pain not responding to simple analgesia and for pathological fractures, and for spinal cord compression complicating extradural plasmacytoma,
- Bisphosphonates, intravenous zoledronate.
Prognosis

• High B2-macroglobulin and low albumin are features of bad prognosis.
• Over one third of patients survive for 5 years.