Treatment options in Myeloma

‘myeloma for the elderly care specialist’

Dr Richard Soutar,

Consultant in Haematology and Transfusion Medicine,

Beatson Oncology Centre, Glasgow and The Scottish National Blood Transfusion Service
• 1. Myeloma – reminder of what it is

• ‘Fancy’ haematological diagnostic criteria -WHO

• Clinico-pathological diagnosis – based on (generally) a clonal immunoglobulin / or part of immunoglobulin and clinical features derived from that protein

• So its differs from most oncology / haematoo- oncology and therefore potential for diagnostic error in either direction!
Myeloma: the pathology (1)
Myeloma: the pathology (2):
the clonal protein: protein electrophoresis

Watch out for light chains, watch out for immunoparesis
2. The clinical features
Skeletal damage
Bone pain (70%)

- Back and rib pain
- Bone with active bone marrow tends to be affected
- Plasma cells produce “OAF” which alter bone turnover
- Produce lytic lesions, osteopenia, fractures, pain, hyperCa++
A paraprotein + osteopenia / wedge # does not = myeloma and a marrow examination often does not help diagnose
Spinal MR image – same patient – much more helpful than doing bone marrow aspirate to get $\Delta$
Myeloma and the kidney: “cast nephropathy”

Low power

High power

And paraprotein + renal impairment does not = myeloma and marrow examination looking at the wrong tissue!
Infections

- Due to reduced immunity: lymphopenia, hypogammaglobulinaemia, high dose steroid
- Recurrent infections
- Serious infections – most commonly pneumonia
- Often not neutropenic but doesn’t mean not prone to problems: Flu, RSV etc.
Hyperviscosity

- Visual disturbance
- Headaches
- Bleeding
- Drowsiness
- Doesn’t have to be IgM, can be IgA, IgG
- Depends on symptoms
  > plasma viscosity
- Responds well to TPE

Retina with papilloedema, dilated veins and haemorrhages
Myeloma: median age 67, incidence 50 per million ~ 1% of cancer
Incidence of multiple myeloma in the UK is rising (per 100,000)
Myeloma Survival Scotland 1987-2011

Survival %

ISD Scotland Data
Great but why?

1960’s alkylating agents – Melphalan

then 20 years of relative stagnation!
Myeloma survival: N E Scotland 1968-72; 83-87

% survival

years

0 1 2 3 4 5

1968-72

1983-87

BGS Oncogeriatrics 2018
So what happened then?

Treatment

**Supportive care:**
- importance of fluid
- bisphosphonates

**Chemotherapy:**
- Stem cell therapy in the “young” < 65-70 years (initially split “to auto or to not to auto”)
- “Novel” therapies
Supportive care: importance of fluid

MRC III: Dacie et al, B J Cancer, 1980, 42, 823
MRC IV: MacLennan et al BMJ 1984
Supportive care: bisphosphonates

Zolendronic acid principally used bisphosphonate

• reduces pain
• reduce pathological #s
• reduce hypercalcaemia
• reduce need for XRT
• improves survival ~ 6 months (MRC Myeloma IX)
Supportive care:

- Team approach: haematology, radiology, renal
- Specialist Nursing
- Palliative Medicine
- Myeloma UK patient support charity
- Care of the elderly:
  - < 60 years: 20% ≥ 1 co-morbidity
  - 60-69 years: 43% ≥ 1 co-morbidity
  - >70 years: 61% ≥ 1 co-morbidity

Co-morbidity has major affect on the principal treatment decision:

*To ‘autograft’ or not to ‘autograft’*

Autograft: Autologous, haematopoietic stem cell transplantation using previously mobilised and collected haematopoietic stem cells
The role of autologous stem cell transplantation - Myeloma VII (OS)

At median f/u 5.5yrs

- Median survival benefit of 14.1 months in intensive arm (56.3 v 42.2m)

Child et al, NEJM, 2003; Morgan et al 2004
‘Novel’ therapies in myeloma

- ‘Imids’
- Proteasome inhibitors
- HDAC inhibitors
- Reliance on potent steroids
- Monoclonal Antibodies
Novel therapies Focus on the biology of the myeloma cell and its microenvironment

- IL-6
- ICAM-1
- VCAM-1
- VEGF
- TNFα

Myeloma cells

Osteoclast

Immune effector cells

Stroma

VEGF

CD38
proteosome

IL-6

ICAM-1
VCAM-1

TNFα
VEGF
‘Novel’ therapies in ‘UK’ myeloma practice

2003 -2007
Imids: Thalidomide, Lenalidomide (‘Revlimid’)
Proteasome inhibitor: Bortezomib (‘Velcade’)

2013 – 2017
HDAC inhibitor: Panabinostat (‘Fardyak’)
Imid: Pomalidomide (‘Imnovid’)
Proteasome Inhibitors: Carfilzomib, Ixazomib
Monoclonal antibody: Daratumumab
New treatments in myeloma

• Thalidomide, usually used as part of a ‘triplet’
• Part of initial therapy in transplant eligible ‘VTD’ and ineligible ‘MPT’ or ‘CTDa’ regimens
• no myelosuppression
• teratogenic
• Thrombogenic
• Peripheral neuropathy – not suitable for ‘maintainence’
New treatments in myeloma

Bortezomib (‘Velcade’)

• Again used as ‘triplet’
• Limiting neuropathy: often autonomic
• Given s.c. overcome many of side-effects than when given i.v.
• Novel “triplet” therapy: biological agent, alkylating agent and steroid have increased response rates from 50-60% to 80-90%
• CR rate from 3-8% to upto 70% with a stem cell transplant
• “Novel” agents can overcome adverse cytogenetics
• But remains incurable
• Continuous ‘maintenance’ therapy
• The issue of increasing issue of cost
Finish