Guidelines for Standard Investigative Workup

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Minimal Diagnostic and Prognostic Evaluation for Multiple Myeloma

- History and physical examination
- Complete blood count and differential; peripheral blood smear
- Chemistry screen including calcium and creatinine
- Serum protein electrophoresis, immunofixation
- Nephelometric quantification of serum immunoglobulins
- Routine urinalysis, 24 hour urine collection for electrophoresis and immunofixation
- Bone marrow aspirate and/or biopsy
- Cytogenetics (metaphase karyotype and FISH)
- Radiological skeletal bone survey including spine, pelvis, skull, humeri and femurs. Magnetic Resonance Imaging in certain circumstances
- Serum B2 microglobulin and lactate dehydrogenase
- Measurement of serum free light chains

History And Physical Examination

- **Past medical history**
  - CAD, CHF, DVT, hypertension, renal disorders, liver disorders, lung disease etc
- **Family history**
  - focus on first degree relatives with the diagnosis of hematologic malignancies especially lymphoma, CLL, and plasma cell dyscrasias
- **Look for AL-amyloidosis**
  - Peripheral neuropathy, carpal tunnel syndrome, organomegaly and signs of nephrotic syndrome

Minimal Laboratory Evaluations

- **Complete blood count with differential**
  - Peripheral smear for rouleaux formation, plasma cells
- **Complete biochemistry**
  - LFTS, urea, creatinine, electrolytes, calcium, albumin
- **Albumin**
  - Nephelometry: most accurate but not widely used
  - Densitometry from SPEP: high concentrations of m-protein may overestimate serum albumin
  - Biochemistry (Bromcresol): good correlation with nephelometric quantitation
- **All albumin methods perform similarly in predicting survival and may be used for ISS**
- **Urinalysis**

Evaluations Of Serum Monoclonal Protein

- **Serum Electrophoresis**
  - Agarose gel electrophoresis or
  - Capillary zone electrophoresis of serum
- **Quantitation of serum immunoglobulins by nephelometry**
- **Measurement of monoclonal protein both by densitometer tracing and by nephelometric quantitation**

Evaluations Of Serum Monoclonal Protein

- **Nephelometric quantitation**
  - may overestimate the m-protein when its value is high
  - useful for low levels of monoclonal IgA, IgM, IgD (not IgG)
  - useful to measure levels of uninvolved immunoglobulins
- **Serum Immunofixation Electrophoresis (IFE)**
  - Gold standard to confirm monoclonal protein and to identify heavy and light chain (routine: IgG, IgA, IgM, κ, λ)
  - should be performed when there is hypogammaglobulinemia
  - should be performed when electrophoretic pattern appears normal but clinical suspicion of PCD
  - If serum IFE +ve for free light chain only do IFE for IgD and IgE

Evaluation Of Urine Monoclonal Protein

- **For suspected or established myeloma collect 24 hour urine**
  - calculate amount of proteinuria
  - calculate creatinine clearance
- **Aliquot from concentrated 24 hour specimen → electrophoresis and immunofixation**
- **Morning urine sample cannot replace 24 hour urine collection**

Serum Free Light Chains

- Recommended in all newly diagnosed patients with PCD
- Very useful in non-secretory, oligosecretory and light chain only myeloma
- SBP, MGUS, SMM → abnormal FLC ratio is associated with higher risk of progression to symptomatic MM
- FLC does not obviate need for 24 hour urine collection
- Urine free light chain assay is not recommended

Bone Marrow Studies

- BM aspirate and/or biopsy are mandatory
- Diagnosis of MM is confirmed if >10% clonal plasma cells
- Clonality → clg by immunoperoxidase or immunofluorescence
- BM biopsy may be preferable
- When both are performed → record the highest number of PC

Cytogenetic Studies

- **Standard metaphase cytogenetics**
  - Low yield; abnormal karyotype ~30%
  - Still prognostic

- **FISH on sorted plasma cells**
  - Probe for t(4;14), t(14;16) and 17p13

Other Tests for Prognosis

- Serum b2-microglobulin: ISS
- Serum LDH: useful in risk assessment
- C-reactive protein → not useful in risk assessment but helpful when infection is suspected

Imaging Studies in Myeloma

- **Skeletal survey**
  - PA chest, AP and lateral skull, C, T, L spine,humeri, femora and AP pelvis
- **MRI**
  - SBP: mandatory MRI of spine and pelvis
  - SMM: recommend MRI of spine and pelvis
  - Symptomatic myeloma:
    - May be performed as a routine evaluation of spine and pelvis
    - MRI mandatory to evaluate symptomatic patient to rule out nerve root or spinal cord compromise
    - to differentiate osteoporotic from myelomatous compression fracture of spine
  - MRI may have prognostic significance

Imaging Studies in Myeloma

- **PET-CT**
  - Definite role is yet to be defined
  - Helpful for detection of extramedullary involvement

Other Diagnostic Considerations

- **Anemia out of proportion of tumor load: look for other causes**
- **Hypercalcemia without typical bone lesions**
  - R/O hyperparathyroidism
- **Consider AL when non-selective proteinuria, low ECG voltages, LVEF, CHF, hepatomegaly, elevated AP, GGT, carpal tunnel syndrome, peripheral or autonomic neuropathy**
- **Consider MIDD when non-selective proteinuria and no evidence of AL**

Follow-up Investigation After Therapy

- Repeat serum and urine studies of monoclonal protein
- Bone marrow aspiration and/or biopsy is needed only to confirm CR
- No need to repeat metaphase karyotype, FISH, flow cytometry, bone imaging as a routine follow-up

Tests To Be Performed At Relapse

- Repeat serum and urine studies of monoclonal protein
- Prognostic significance of b2 microglobulin or ISS is unclear
- Elevated serum LDH confers poor prognosis
- Skeletal survey is indicated to detect possible lesions at risk for fracture
- Other imaging studies: only if clinically indicated

Tests To Be Performed At Relapse

- **Bone marrow aspirate and/or biopsy**
  - should be performed if suspicion of hyposecretory progression or of MDS
  - Karyotype and FISH
  - If not performed at baseline → should be done
  - If performed at baseline and normal→repeat
  - If performed at baseline and abnormal with high risk feature → no need to repeat