Shared Care MGUS

Presenters

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WINDSOR REGIONAL HOSPITAL

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Objectives

- Define MGUS and discuss high risk versus low risk MGUS
- Discuss shared care for MGUS between family physician, internist and hematologist
- Discuss conditions that can be associated with MGUS: lymphoplasmacytic lymphoma, peripheral neuropathy, amyloidosis

MGUS

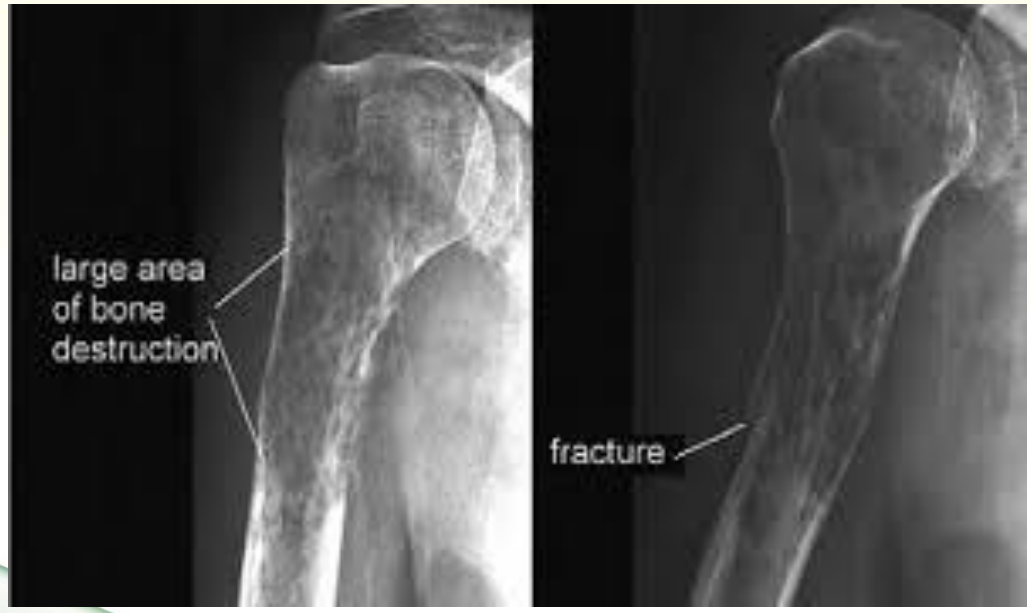
- Serum M protein < 30 g/L
- < 10% clonal plasma cells in the bone marrow
- Absence of end-organ damage that can be attributed to the plasma cell proliferative disorder

Smoldering/Asymptomatic MM

- Monoclonal protein level of 30 g/L or more or urinary monoclonal protein of >/=500mg/24hrs and/or
- Proportion of clonal plasma cells in the bone marrow of 10%-60%
- No end-organ damage (CRAB)
- 10% per year risk of progression to symptomatic MM in the first 5 years

Symptomatic/Active Multiple Myeloma

- Clonal bone marrow plasma cells or biopsy proven bony or extramedullary plasmacytoma and any of the CRAB features or Myeloma defining Events (MDEs)
- CRAB:
  - Hypercalcemia
  - Renal Impairment
  - Anemia
  - Bone lesions



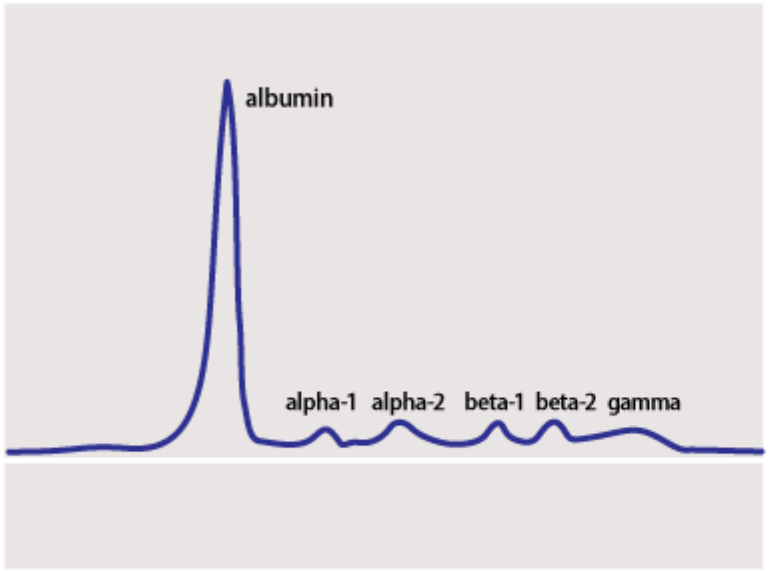
MDEs

- 60% or greater clonal plasma cells in the BM
- Serum involved/uninvolved free light chain ratio >/= 100
- More than one focal lesion on MRI at least 5mm in size

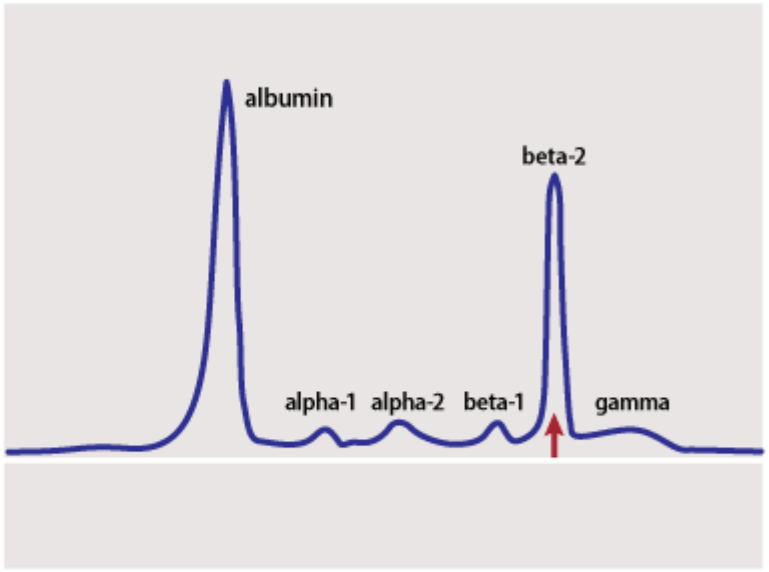
Investigations

- Immunoglobulin levels (IgG, IgA, IgM)
- SPEP (monoclonal protein) and Immunofixation (type)
- Serum free light chains
- UPEP and Immunofixation
- Imaging (skeletal survey/x-ray, CT, MRI, PET)

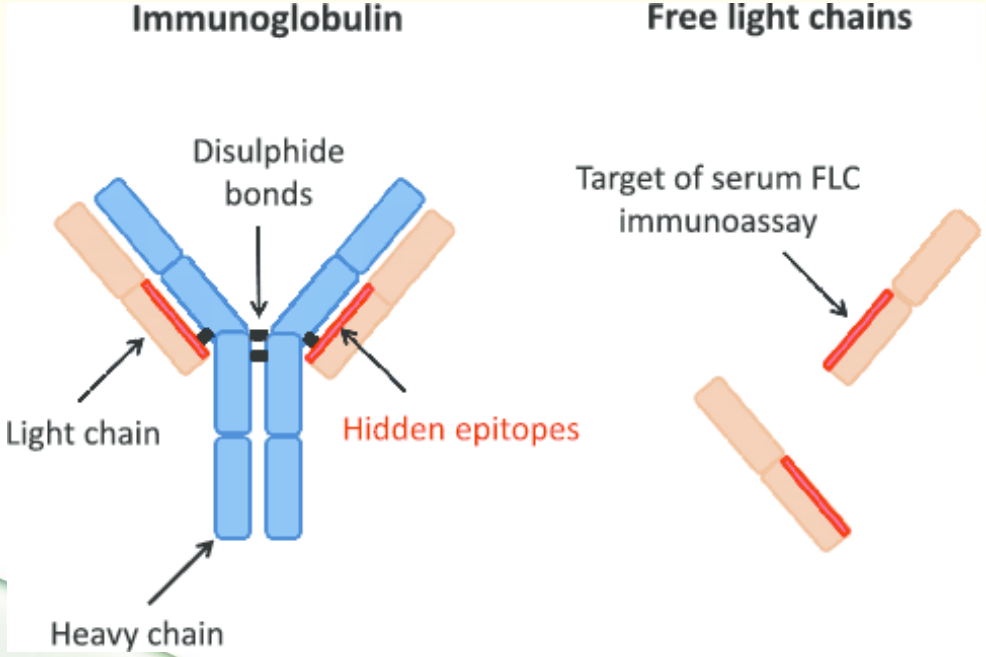
SPEP Test Results



Normal SPEP result



Abnormal result with myeloma cells producing the M-protein, creating an M-spike in the beta-2 zone



Shared Care Model

KEEP, SKIP, LET GO…

- KEEP: One time evaluation by hematologist with subsequent follow up by family MD/internist

- SKIP: follow up both by hematology and family physician/internist

- LET GO: follow up and treatment mainly at the cancer center

KEEP

#1. 65 y/m with pmhx of HTN was being evaluated for minimally elevated total protein and found to have the following labs:

- CBC unremarkable, Creatinine normal, Calcium normal, SPEP and IF showed IgG kappa at 10gm/l, FLC: free kappa 25 (minimally elevated), Free lambda normal, ratio normal.

- Low Risk MGUS International Myeloma Working Group
  - M protein < 15 g/L
  - IgG type and
  - Normal free light chain (FLC) ratio

- Referred for hematology evaluation

- Hematology evaluation:
  - No evidence of end organ damage
  - No peripheral neuropathy
  - No signs and symptoms suggestive of amyloidosis

- No need for Bone marrow biopsy or skeletal survey (low risk MGUS)

- Risk of progression to MM around 1% per year

Recommendation:

- Discharge to family physician/internist
  - Follow up SPEP in 6mo and then every year or two
  - Refer back when patient develops smoldering myeloma or any suspicion of end organ damage
  - BM when high risk MGUS
- Could also be seen occasionally by hematology (shared visit)

SKIP

2. 75 y/f with PMH of HTN, DM had work up for mild renal impairment:

- CBC unremarkable, Cr. 120, GFR 55ml/min, calcium normal, SPEP and IF showed M-protein of 22gm/l, IF IgA lambda
- FLC : free kappa 25, Lambda 100 (elevated), ratio 0.25

- High risk MGUS and mild renal impairment
- Has additional risk factors for renal impairment (HTN, DM)
- Referred for hematology evaluation, bone marrow biopsy and follow up

Hematology evaluation:

- Bone marrow aspiration and biopsy (morphology, flow, cytogenetics (karyotype and FISH) showed 9% monoclonal plasma cells.
- Skeletal survey: degenerative changes, no lytic lesions.
- Recommend shared follow up every 6months: CBC, electrolytes, Calcium, SPEP, IG levels, FLC

Risk Stratification for MGUS

Low-risk:

- Serum M protein <15 gm/L, IgG subtype, normal FLC
- Absolute risk of progression to MM in 20yrs 5%.

Low-intermediate-risk:

- Any 1 factor abnormal

High-intermediate-risk:

- Any 2 factors abnormal

High-risk:

- All 3 factors abnormal
- Absolute risk of progression to MM in 20yrs 58%!

- Remember pts with high risk MGUS could have:
  - Recurrent Infection
  - Osteoporosis
  - Peripheral neuropathy (rare, usually IgM)
- Evaluate for signs and symptoms of amyloidosis
- Watch high risk patients for any evidence of end organ damage
- Remember non secretary myeloma and isolated plasmacytoma

Let Go

3. 75 y/f with PMH of HTN, DM had work up for mild renal impairment which resolved after hydration, labs showed:

- CBC unremarkable, creatinine normal, calcium normal, SPEP and IF showed M-protein of 32gm/l, IF IgA lambda
- FLC : free kappa 10, Lambda 1050 (very high), ratio of involved vs uninvolved =105

- BM biopsy showed 65% monoclonal plasma cells
- Skeletal survey negative for lytic lesions
- Patient counseled on diagnosis and initiated on anti-myeloma therapy
- FLC ratio (100 or more) and BM clonal plasma cells (60% or more) are both indications for treatment initiation

- Initiate anti-myeloma therapy in patients with any of these:
  - Involved versus uninvolved FLC ratio 100 or more
  - BM clonal plasma cells 60% or more
  - 2 or more focal lesions on MRI

- These patients have 80% or more risk of progression to active myeloma in 2 years!

- Ultra-high risk SMM (IMWG, Lancet 2014)

LET GO

#4. 76y/m with mild renal impairment has labs:

- CBC moderate anemia, Cr 120, GFR 50ml/min, calcium normal, SPEP M protein of 10g/l IgM kappa with elevated total IgM.
- Further evaluation showed bilateral axillary nodes, history of night sweating and weight loss
- CT scan: generalized lymphadenopathy
- Referred for hematology evaluation

- Bone marrow biopsy:
  - Clonal plasma cells 8%
  - B cell lymphoproliferative disorder

- Diagnosis: lymphoplasmacytic lymphoma/Waldenstrom's macroglobulinemia

- Treatment initiated because of anemia

- Conditions to consider/exclude in IgM MGUS:
  - Lymphoplasmacytic lymphoma
  - AL amyloidosis
  - Peripheral neuropathy (rare)

- Work up for amyloidosis if there are suspicious signs and symptoms (fat pad, BM, potentially involved organ biopsy)

5. 32y/f on HD for ESRD developed abdominal pain. Work up showed massive hepatomegaly, anemia, SPEP no monoclonal protein, FLC elevated lambda 1515, kappa 96, k/L ratio 0.06

Summary:

- Elevated FLC
- Massive hepatomegaly

Amyloidosis suspected:

- Bone marrow congo red stain was negative
- Abdominal fat pad biopsy negative
- Liver biopsy showed amorphous material suspicious for amyloid
- Mass spectrometry (send out test to PMH) confirmed Al amyloidosis
- Patient doing well for >1 year on chemotherapy

Signs and symptoms suggestive of amyloidosis in MGUS that need further work up:

- Nephrotic range proteinuria, renal failure
- Unexplained heart failure (may need myocardial biopsy)
- Unexplained peripheral neuropathy
- Unexplained hepatosplenomegaly
- Unexplained chronic diarrhea
- Unexplained bruising/bleeding…

Thank you

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