Disease Morbidities 2; IgM related disorders, renal, hyperviscosity & Cryos

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We had an amazing conference:
Thank you everyone!
Rembrandt van Rijn 1606-1669 – Anatomy Lesson

Dokter Tulp
Complications of WM

- IgM related disorders: even when there are not many tumour cells, the IgM can still be tricky
- Hyperviscosity – when the blood is too sticky
- Cryo’s: when the blood clots in cold
- Renal disease related to WM: can the kidneys suffer from WM?
IgM related Disease

- Waldenstrom’s disease: high tumor load in the bone marrow, high IgM; symptoms arise because of the tumour (i.e. anemia, hyperviscosity)

- IgM related disease: low/no tumor load in the bone marrow, low IgM but this little bit of disease leads to (sometimes severe) symptoms “dangerous small clone”.
Types IgM related disease (typically IgM MGUS)

- Deposition diseases:
  - amyloidosis, light chain deposition, IgM deposition

Neuropathy

Nephropathy- kidney disease

Cryo’s

Cold agglutinins

Schnitzler syndrome (skin)
How to treat

- Depends on the type of IgM related disorder
- Most will be discussed today
Hyperviscosity

Probably the most dangerous complication of WM
What is viscosity
Let’s remember: why is it called macroglobulinaemia? Because it’s so big!
Hyperviscosity syndrome

- Described in 1944 in the initial 2 patients identified by J.G. Waldenstrom
- High IgM makes the blood too thick
- mostly at IgM > 6 g/dL - 60 g/L but possible from 3 g/dL – 30 g/L
- This can lead to
  - Bleeding (nose, other mucous membranes, skin)
  - Retinopathy – damage to the retina in the eye
  - Neurological problems
Symptoms and signs: sausasing of the retinal vessels – hotdogs on a string
How to diagnose

- IgM paraproteine
- Viscosity testing of the blood (although….)
- Clinical awareness of symptoms
- Funduscopy (“eye exam”)
How to treat?

- Plasmaferesis!
- "Wash" the blood to filter out the IgM
- Via central line

KEEP CALM AND PLASMAPHERESIS
For how long

- Sessions every day-couple of days-weekly
- Untill the IgM is brought down by rapid acting treatment
New during IWMM9

- No new insights, but more and more rapidly effective agents available!
What are cryoglobulines?

- Proteins that precipitate in cold circumstances
- Typically, 3 types are distinguished:
  - Type 1: monoclonal IgM or IgG -> WM/IgM MGUS, other lymphoma’s
  - Type 2: monoclonal IgM with polyclonal IgG -> hep C
  - Type 3: polyclonal IgM/IgG -> auto-immune diseases (lupus, RA)

- Type 1: WM/MGUS, lymphoma
- Type 2/3: Hepatitis C, autoimmune diseases (lupus, RA), But sometimes also lymphoma
Anecdote courtesy of dr Marvin Stone
Symptoms of cryo’s

- Purpura
- Acrocyanosis
- Ulcera-poor wound healing
- Mostly on extremities- where the vessels are small and the blood cools (shins, ears, nose, fingertips)
Cryoglobulinines

Can falsely lower the IgM when not testing in warm bath!!

(or in warm room – dr Eva Kimby, Karolinska institute Stockholm, Sweden)
Complications of cryo’s

- Mild symptoms (most frequent)
- Purpura (bright red circles, from the size of a pinhead up to half an inch)
- Poor wound healing
- Kidney problems
- Hyperviscosity (because of the immune complexes/precipitation)
- Joint pain/swollen joints
- Neuropathy
What can you do about cryo’s?

- Stay warm
- Take care / keep an eye on ulcers or wounds
- Inform your physician/nurse if you have cryo symptoms
- Sometimes hep C needs to be tested

- Mild -> wait & see, monitoring
- Severe
  - -> treatment of underlying disease
  - -> sometimes pheresis (in a warm room!)
New during IWWM9

- We now know there’s a warm room in Karolinska institute!
WM related nephropathy

- Kidney complications related to WM
Why check urine in WM?
The kidney filters the blood: 1 liter/minute!
Renal complications in WM

• Up to 5% of patients on 15 years of follow up

• Great variety in WM related renal disease

• Renal disease is not always related to WM! (Diabetes, hypertension)

• Sometimes a biopsy of the kidney will be needed to determine the cause

1) Chauvet et al AJKD 2015, 2) Vos et al, BJH 2016
What are the symptoms of renal disease

- Renal failure – no symptoms until it’s very advanced (fatigue, not feeling well)
- Nephrotic syndrome (proteine leakage) – edema also in the face
- “tubulopathy” – disturbances in the salt in the blood – muscle cramps, typically asymptomatic and picked up by routine lab
Renal complications in WM: many different types; based on kidney biopsies

- Amyloidosis \( (n = 11) \)
- IgM deposition/cryoglobulinaemia \( (n = 10) \)
- LPL infiltration \( (n = 8) \)
- Light chain deposition \( (n = 4) \)
- Light chain cast nephropathy \( (n = 4) \)
- Thrombotic microangiopathy \( (n = 3) \)
- Minimal change disease \( (n = 2) \)
- Light chain tubulopathy \( (n = 1) \)
- Membranous nephropathy \( (n = 1) \)
What else do we know

• 50% of cases diagnosed together with WM diagnoses, but can occur up till 10 years later

• WM’ers with kidney complications have somewhat poorer outcomes

• If renal function is saved then outcomes are better

• Hematologist/oncologist needs to cooperate closely with kidney specialist (nephrologist)

• Optimal treatment unknown and very dependent on exact type of kidney disease
Monoclonal IgM deposition disease (McPhee) often has a mild clinical course with relapses over the years.
What can you do about kidney complications

- Monitoring kidney function (typically part of standard blood testing)
- Check the urine for proteine
- Be aware of symptoms (only nephrotic syndrome)
- Doctors should be aware this can be associated with WM/IgM MGUS and make the proper investigations
New on IWWM9

- Recent published analysis of data from the Bing Center cohort was discussed (based on 1391 WM patients)
Thank you & enjoy your time in The Netherlands

Gerard Dou’s doctor is @ Rijksmuseum, Amsterdam

Rembrandt’s Anatomy lesson is @ Mauritshuis, The Hague.