W28: IgM Smouldering Mutiple Myeloma in a young patient over six years follow-up: case report of an extremely rare hematologic entity

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Background

IgM myeloma is an extremly rare subtytpe of MM (prevalence 0.5); more rare is IgM Smouldering Mutiple Myeloma (IgM-SMM), a pre-malignant condition with an inherent risk for progression. Due to its rarity, there is a lack of studies and a debate still open about knowledge and definition. We present a case of IgM-SMM in a young patient over six years follow-up.

Case report

In February 2012 asymptomatic 42-year-old woman presents incidental monoclonal peak. The work-up that follows (table I) is conclusive for IgMƛ- SMM, according to IMWG criteria. A "watch and wait" strategy is decided, with a close follow-up every six months. Since 2014, according to the revised criteria for definition of active MM, the work up has investigated also the MDEs. After more than six years the patient is well and the disease remain unchanged, without progression.

Discussion

Diagnostic assessment.

IMWG guidelines define subtype IgG/IgA-SMM as a monoclonal gammopathy disorder with serum monoclonal protein ≥30 g/L or urinary monoclonal protein ≥500 mg/24h and/or clonal bone marrow plasma cells 10–60%, without any end-organ-damage or MDEs or amyloidosis (Rajkumar *et al*, 2014); still debated is the definition of IgM-SMM. The diagnosis of IgM-MM currently requires the presence of IgM monoclonal gammopathy, ≥10% bone marrow plasma cells, lytic bone lesions and/or translocation t(11;14) (Schuster SR, Am J Hematol 2010). This strict definition can misdiagnose IgM patients, in wich pure clonal bone marrow plasma cell infiltration and immunophenotypic data are suggestive of MM, but in wich there are not cytogenetic abnormalities and/or lytic lesion (Owen RG, , Am J Hematol 2011). Due the overlapping of clinical presentations between IgM-MM and Waldentrom Macroglobulinemia (WM), the presence of IgM-monoclonal gammopathy and bone marrow biopsy alone is not enough to an accurate diagnosi. The presence of a somatic mutation MYD88-L265P in patients with WM and the absence of it in cases of myeloma, including IgM-secreting-myeloma, allows to distinguish these two entity. Based on these assessments about diagnostic criteria, this patient's disease is surely IgM-SMM

Prognostic evaluation

Risk factors for progression of SMM are considered: clonal BMPCs 50-60%, M protein > 30 g/L, IgA M component, immunoparesis, SFLC ratio 8-100, rising M protein (>25% increase on 2 evaluations within 6 months), t(4;14) or del(17p) or +1q, skeletal MRI with 1 lesion

(Rajkumar et al, Blood 2015). Recent evaluation showed that M subtype of MM per se does not affect prognosis.

Risk of progression to malignancy, in retrospective review of 276 pt with SMM at Mayo (1970-1995), was: 10%/year for the first 5 years, 3%/year for next 5 years, 1%/year thereafter. Our patient has at low/intermediate risk.

Therapeutic challenge

Newer prognostic markers allow to risk-stratify SMM/MM: for patients with low/inermediate risk close surveillance remains the standard of care, outside clinical trials.

Conclusions

In impressive new knowledge era, the closely "watch and wait" strategy in SMM low/intermediate risk young patients avoids them useless toxicity, waiting for more effective therapy (long survival/healing?) and minimal adverse effect.

Table I. Patient Characteristics

Age	41
Sex	F
Clinical presentation	asymptomatic
Clinical examination	negative
IgM spike (g/L)	48.100
IgG (g/L)	3,560
IgA (g/L)	0,250
Light chain type (κ/ʎ)	ʎ
Ca (mg/dl)	9,4
Creatinina (mg/dL)	0,7
Hb (g/dl)	11.6
MRI (bone lesion)	NO
Bone marrow (% clonal PC)	45
Flow cytometry (BMPC)	CD38++, Cd19-, Cd45-, CD56-
Cytogenetic (FISH)	normal female karyotype
SFLC (involved/uninvolved ratio)	16
β2 microglobulina (ng/ml)	1434
MYD88:	wild type
Paraombelical fat (red Congo)	negative
ProBNP (pg/mL)	30
Cardiac Troponin I (pg/ml)	1
Ocular fundus	Normal