Non-IgM Secreting Lymphoplasmacytic Lymphoma

Experience of a Reference Center for Waldenström's Macroglobulinemia

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Background

- Lymphoplasmacytic lymphoma (LPL) secreting immunoglobulins other than IgM is rare
- There are very few case series on non-IgM LPL and little is known about the clinical features and outcomes of patients with this disease.

Aim

To describe disease characteristics and clinical outcomes of patients with non-IgM LPL

Methods

- We identified cases of non-IgM LPL in the records of the Waldenström's Macroglobulinemia (WM) clinic at our institute, between the years of 2000-2018.
- All patients were part of the clinic registry
- We extracted data from their electronic records and included only cases with centrally-confirmed diagnosis
- Response assessment was based on 6th IWWM criteria
- Time to events was estimated using the Kaplan-Meier method

Results - Patient Characteristics

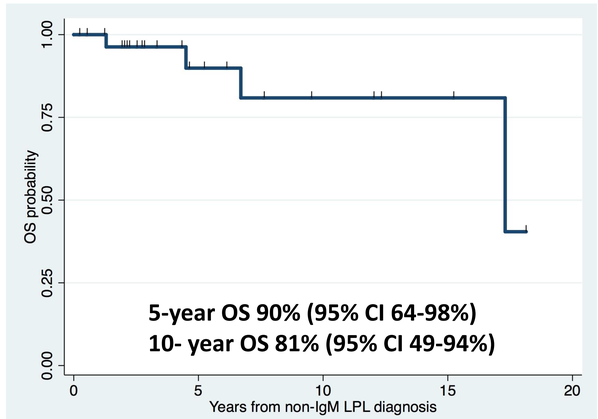
- We found 31 patients who met diagnostic criteria, with prevalence of ~1.3% of the Bing Center patient population
- Their clinical characteristics are depicted in Table 1
- We included 5 cases with concurrent IgM paraproteinemia, when it was clearly secreted to a lesser extent than dominant IG and had similar LC restriction.
- Albeit small numbers, there was no apparent difference between patients with IgG and non-IgG secretion.

Total	31 patients
Age – Median	63 years (37-83)
> 65 y	45%
Sex	65% ♀
Paraprotein	
IgG	20 (65%); 3,967 mg/dl (804-8,006)
IgA	5 (16%); 1,980 mg/dl (1,020-6,210)
Light chain	2 (6%)
Non-secretory	4 (13%)
Light chain restriction	Kappa in 25/30 (83%)
Preceding MGUS	5 (16%)
Presentation	
Asymptomatic	7
Anemia-related	11
Autoimmune	3
Bleeding diathesis	3
Elevated creatinine	3
Recurrent infections	3
B-symptoms	1
Hyperviscosity[$]	1
Imaging	
Lymphadenopathy	11 (35%), all < 5 cm
Splenomegaly	5 (16%), all mild
Laboratory	
Anemia – any	53%
Hb < 10 g/dl	23%
ANC < 1 or PLT < 100K	none
Lymphocytosis	16% (median 7.1 K/ul; 3.3-20.6)
β2MG > 3 mg/L	48%
Pathology	
BM flow cytometry	CD20+ in all, CD5dim/subset in 14%, CD23dim/subset 29%, CD10 negative in all
Cytogenetic abnormalities	5/19 (26%)^
Amyloidosis (AL)	2
LCDD	1
MYD88[L265P] mutation	10/14 (71%)
CXCR4[WHIM/FS] mutation	2/8 (25%)

Table 1. [$]As retinal vein occlusion, IgA 4,000 mg/dl, ^ Del6q (n=1), otherwise none commonly known aberrations in heme malignancies. *BM, bone marrow; LCDD, LC deposition disease.*

Results – Disease Course and Therapy

- Median follow up was 4.6 years (95% CI 2.5-7.6 years)
- 68% of the patients had been treated (n=21), 90% of whom within the first year from diagnosis.
- Median time to first treatment was 2.3 months
- Median time to second therapy was significantly longer @ 4.7 years.
- Patients received a median of 3 lines of therapy (range, 1-8) including
  - Purine analogues (33%), alkylating agents (48%), bendamustine (38%), anti-CD20 monoclonal antibodies (90%), proteasome inhibitor (24%), immunomodulating drugs (14%), and ibrutinib (n=2).
  - 1 pt on ibrutinib achieved VGPR, after 7 prior therapies, with over 3 years remission duration. The other had a brief response, and was found to carry the CXCR4 mutation.
  - Interestingly, both patients with a CXCR4 mutation needed therapy immediately at diagnosis and subsequently had 4 or more lines of therapy.
- 4 pts died (13%): 1 from Bing-Neel syndrome; 1 with treatment complications; and 2 of unknown cause.



Conclusion

To our knowledge, this is the largest reported series of non-IgM LPL and the first to demonstrate excellent long-term outcomes in these patients.

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There are no relevant relationships to disclose