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The Natural History of Asymptomatic (Smoldering) Waldenström Macroglobulinemia (WM): Factors Predicting Progression to Symptomatic WM and Transformation

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INTRODUCTION

- WM is a rare, complex hematological malignancy.
- Patients with WM are divided into asymptomatic (smoldering) and symptomatic.
- The natural history of WM is not well described.
- Some patients present with a rapidly progressive disease versus others who are diagnosed during routine checkup and remain asymptomatic.

AIM

To evaluate factors that can predict progression to symptomatic WM and transformation.

METHOD

- Single Center Retrospective Study.
- Data collected on 265 patients who presented to Moffitt Cancer Center with diagnosis of WM between 1995 and 2020.
- We divided our patients into 3 cohorts based on the natural history of their disease progression pattern: (1) patients who remained asymptomatic, (2) patients who progressed from asymptomatic to symptomatic WM, and (3) patients who transformed from asymptomatic to diffuse large B-cell lymphoma (DLBCL).

RESULTS

- Our study included 265 patients who presented to Moffitt Cancer Center with diagnosis of WM between 1995 and 2020.
- 52% of the patients (n=138) were asymptomatic versus 48% (n=127) were symptomatic at time of diagnosis.
- The mean age at diagnosis was 68 years for asymptomatic patients and 76 years for symptomatic patients.
- During the 26-year study, with a median follow-up of 9.7 years, 58% (n=80) progressed to symptomatic WM versus 42% (n=58) remained asymptomatic.
- Clinical and laboratory risk factors for progression (Table 1) included male sex (*P*<0.001), low hemoglobin <12.5 g/dL (*P*=0.02), IgM level >3 g/dL (*P*<0.001), albumin <3.5 g/dL (*P*=0.01), and beta-2 microglobulin >4 mg/dL (*P*=0.001).
- Pathologic risk factors for progression (Table 1) included bone marrow lymphoplasmacytic infiltration >60% (*P*=0.01).
- The rate of transformation to DLBCL was 3.7% in symptomatic patients and 2.5% in asymptomatic patients (*P*=0.02).

Table 1. Clinical, laboratory and pathologic risk factors for progression.

Risk Factors	P-Value
Male sex	(*P*<0.001)
Low hemoglobin <12.5 g/dL	(*P*=0.02)
IgM level >3 g/dL	(*P*<0.001)
Albumin <3.5 g/dL	(*P*=0.01)
Beta-2 microglobulin >4 mg/dL	(*P*=0.001)
Bone marrow lymphoplasmacytic infiltration >60%	(P=0.01)

CONCLUSIONS

- To our knowledge, this is one of the largest cohorts to describe the natural history of WM.
- Patients with WM are more likely to be asymptomatic at time of diagnosis.
- Factors that predict progression to symptomatic disease include male sex, low hemoglobin <12.5 g/dL, IgM level >3 g/dL, albumin <3.5 g/dL, beta-2 microglobulin >4 mg/dL, and bone marrow lymphoplasmacytic infiltration >60%.
- The rate of transformation to DLBCL is less in asymptomatic patients.

REFERENCES

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