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IgM related AL amyloidosis: about 2 cases

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Introduction

IgM-related light chain amyloidosis accounts for less than 10% of all AL amyloidoses and carries a poorer prognosis. Peripheral nerves and lymph nodes are commonly involved in contrast to the heart. Due to the rarity of the disease, prognostic criteria and treatment recommendations are lacking

Results

We report two cases of AL amyloidosis related to a MYD88 positive Waldenström Macroglobulinemia (WM). In both cases, delay between the onset of symptoms and diagnosis was over one year.

The first patient, a 74-year-old man, had a history of 1-year hoarseness for which several investigations remained inconclusive. He developed swallowing problems related to macroglossia and was finally referred for progressive sensitive polyneuropathy leading to the diagnosis of kappa AL amyloidosis related to IgM kappa WM. He failed to respond to R-Cd combination, achieved a partial hematological response after six cycles of R-Bendamustine, and finally obtained an organ improvement under R-Vd.

The second patient, a 54-year-old man, repeatedly complained of shortness of breath that was first attributed to coronaropathy with no improvement after stenting. He had a 5-year history of IgM MGUS. Echocardiography identified a thickening of the ventricular septum leading to the diagnosis of AL lambda amyloidosis. Initial work-up pointed out a cardiac Mayo stage 3. He was successively treated with R-Vd, R-Bendamustine and R-Cd, without any relevant hematological or cardiac response. He finally achieved a complete hematological remission after six cycles of Daratumumab monotherapy, with a progressive improvement of his cardiac function.

	Patients characteristics	
	Patient 1	Patient 2
Age at diagnosis	74 y	53 y
Amyloidosis subtype	AL kappa	AL lambda
Diagnosis delay	15 months	60 months
Main organ	Nerve	Heart
Number of organs involved	2	1
Site of biopsy	Sublingual gland + skin	Heart
Associated disease	Waldenström MYD88 +	Waldenström MYD88 +
Involved chain	IgM kappa	IgM lambda
Number of therapy lines	3	4
First line	R-Cd x 3 cycles	R-Vd x 5 cycles
Response	Failure	PR (+ nerves toxicity)
Second line	R-Bendamustine x 6 cycles	R-Bendamustine x 5 cycles
Response	PR, no organ response	Failure
Third line	R-Vd x 7 cycles	R-Cd x 7 cycles
Response	PR and organ improvment	Failure
Daratumumab based regimen	/	4th line
Response	/	CR and organ improvment

Conclusion

IgM-related AL amyloidosis is a distinct entity with a less favorable outcome compared to non-IgM amyloidosis; therefore, early diagnosis is critical for organ prognosis. Treatment options can be limited by a higher prevalence of polyneuropathy limiting the use of bortezomib. Tackling the lymphoid component of the clone remains the main goal of therapy in order to achieve an adequate organ response.

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