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AN EXPERIENCE OF PRIMARY AMYLOIDOSIS FROM AN INDIAN TERTIARY CANCER INSTITUTE IN SOUTH INDIA

Haematology

Manjunath Nandennavar — Associate Professor, Department of Medical Oncology, Vydehi Cancer Centre, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, 560066.

Gorla Vishnu Priyanka — Senior resident, Department of Medical Oncology, Vydehi Cancer Centre, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, 560066.

Veerendra Angadi* — Assistant Professor, Department of Medical Oncology, Vydehi Cancer Centre, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, 560066. *Corresponding Author

Shashidhar V K — Professor & Head, Department of Medical Oncology, Vydehi Cancer Centre, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, 560066.

ABSTRACT

Introduction: Primary or AL (amyloid Light chain) Amyloidosis is a clonal plasma cell disorder. It is an uncommon disorder and exact incidence is unknown. AL amyloidosis can present with variety of symptoms and signs. There are limited studies about clinical profile, treatment and outcomes of patients with AL Amyloidosis in Indian context. We aim to describe the clinical profile and outcomes of patients with AL amyloidosis in our center. **Materials & Methods:** A retrospective descriptive analysis was carried out on patients with proven AL amyloidosis, treated from October 2013 to August 2022. **Results:** Data from 11 patients was compiled and analyzed. The median age at presentation was 54 years. All patients were males (100%). Most common symptoms were pedal oedema in 8 (72%) patients, shortness of breath in 4(36%) patients, Loss of sensations and tingling of upper and lower limbs in 2(18%) patients and lymphadenopathy in 1(9%) patient. Kidney was involved in 7(63%) patients, heart in 3(27%) patients, peripheral nerve in 2(18%) patients and mediastinum in 1(9%) patient. The induction chemotherapy regimens used were Bortezomib-based in 8(72%) patients, Immunomodulator-based in 2(18%) patients. 2(18%) patients underwent Autologous Stem Cell Transplantation (ASCT). Patients who received bortezomib-based treatment had favourable haematological response (62.5%) compared to those who received non-bortezomib-based treatment (9%). Of 11 patients, 3(28%) patients died and 8(72%) patients are alive. **Conclusion:** This study presents the spectrum of clinical manifestations and outcomes in Indian population. Our study results are in common with the fact that response rates and survival improve with early diagnosis and treatment. Autologous stem cell transplantation should be considered for transplant eligible patients.

KEYWORDS

Amyloidosis, Bortezomib, Transplant.

INTRODUCTION

Primary or AL Amyloidosis is a clonal plasma cell disorder. It is an uncommon disorder and exact incidence is unknown. AL amyloidosis can present with variety of symptoms and signs. Substantial heterogeneity in clinical presentation of AL amyloidosis leads to difficulties in the early and correct diagnosis, as well as special challenges in management [1]. The overall prognosis of AL amyloidosis is poor, because amyloid deposits in multiple organs such as the heart, liver, and kidneys, and lead to organ failure and death. Treatment approaches for Primary amyloidosis focus on suppressing the abnormal plasma cell clone, with the aim of decreasing the production of light chains. Stem cell transplantation should be considered for eligible patients. For patients who are not eligible for transplantation, the standard treatment regimen is based on bortezomib treatment[2] . There are limited studies about clinical profile, treatment and outcomes of patients with AL Amyloidosis in Indian context. We aim to describe the clinical profile and outcomes of patients with AL amyloidosis in our center.

MATERIALS AND METHODS:

A retrospective descriptive analysis was carried out on patients with proven AL amyloidosis, treated from October 2013 to August 2022. Amyloidosis was diagnosed on biopsy by the presence of Congo Red-positive fibril deposition. Immunohistochemistry was done to determine the kappa or lambda light chain specificity of the fibre. Serum Immunofixation electrophoresis, serum-free light chain analysis, Bone marrow for plasmacytosis were done. Blood investigations and work up for organ involvement was done according to standard criteria.

RESULTS

Data from 11 patients was compiled and analyzed. The median age at presentation was 54 years (Table 1). All patients were males (100%). Majority of patients were of ECOG status (Eastern Cooperative Oncology Group Status)-1(81%). Most common symptoms were pedal oedema in 8 (72%) patients, shortness of breath in 4(36%) patients, Loss of sensations and tingling of upper and lower limbs in 2(18%) patients and lymphadenopathy in 1(9%) patient. Kidney was involved in 7(63%) patients, heart in 3(27%) patients, peripheral nerve in 2(18%) patients and mediastinum in 1(9%) patient (Figure 1). One patient was dialysis dependent at presentation. Out of 11 patients, 9(82%) patients had single organ involvement and 2(18%) patients had dual organ involvement.

Investigations showed median Hemoglobin (Hb) was 12.4 g/dl, calcium was 8.7 mg/dl, albumin was 3.11 g/dl, Alkaline Phosphatase (ALP) was 169 U/L, Beta-2 Micro-globulin was 3.27 mcg/dl. Nine (81%) patients had nephrotic range proteinuria with median urine PCR (protein creatinine ratio) of 6.2. The median level of NT proBNP in cardiac patients was 11,914 Pg/ml and Trop I was 0.218 ng/ml. Nerve Conduction Studies were done in 2 patients with peripheral neuropathy which showed sensory and motor axonal polyneuropathy. Out of 3 patients with cardiac involvement, echocardiography showed restrictive cardiomyopathy in 2 patients. Cardiac MRI (Magnetic Resonance Imaging) was done in one patient which showed delayed myocardial enhancement. Bone Marrow Plasmacytosis was present in 72% cases, median bone marrow plasma cells were 10% (IQR-6-15%). Most common site of biopsy was kidney in 7(63%) patients. Two patients had biopsy from sural nerve, one patient from cervical lymph-node. Immunohistochemical staining of amyloid deposits for Light chains: 8(72%) patients stained positive for LAMBDA, 3(28%) for KAPPA (Figure 2).

The Induction chemotherapy regimens used were Bortezomib-based in 8(72%) patients, Immunomodulator-based in 2(18%) patients. Out of 8 patients who received bortezomib based therapy, 5(62.5%) patients had favorable hematological response and 3(37.5%) patients had progressive disease. Both patients who received immunomodulator based therapy had progressive disease (Figure 3). Two patients with renal involvement underwent autologous stem cell transplantation. Out of two patients with dual organ involvement, one had progressive disease, other had partial response. Out of 3(28%) patients with cardiac involvement, two patients had progressive disease after first line treatment and one patient had partial response.

Of 11 patients, 3(28%) patients died and 8(72%) patients are alive (Figure 4).

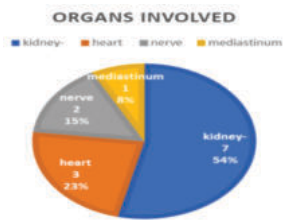

Figure 1

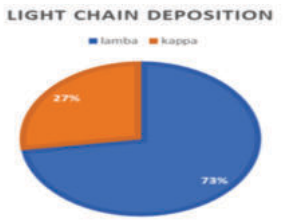

Figure 2

Table 1 Baseline demographic, clinical characteristics and treatment	Patients(n = 11)
Median age(range)	54 (32-68)
Male, n (%)	11 (100%)
ECOG	
1 (n)	9 (82%)
2 or more (n)	2 (18%)
Organ involvement , n (%)	
Renal	7(63%)
Cardiac	3(27%)
Peripheral neuropathy	2(18%)
Mediastinum	1(9%)
Number of organs involved	
1, n	9(82%)
2, n	2(18%)
Light Chain Isotype	
Kappa	3(27%)
Lambda	8(73%)
Proteinuria	
<3.5 g/day	0
>3.5 g/day	9(82%)
Missing	2(18%)
NTproBNP(pg/ml)	
Elevated n, median	4(34%),11914(329-21,110)
Normal ,n	7(63%)
Troponin I(ng/ml)	
Elevated, n median	3(27%), 0.218(0.11- 0.33)
Normal, n	8(73%)
Hemoglobin (g/dl), median (range)	12.3 (9.8-14.3)
Serum Albumin(g/dl), median (range)	3.11(2.38-4.05)
Creatinine (mg/dl), median (range)	2.99(0.5-2.3)
BoneMarrow Plasma Cells, median% (range)	10(6%-15%)
Treatment	
VTD (Bortezomib, Thalidomide, Dexamethasone), n	1(9%)
RD (Lenalidomide, Dexamethasone), n	1(9%)
CyBorD(Cyclophosphamide, Bortezomib, Dexamethasone), n	8(73%)
No treatment	1(9%)
Hematological response	
Partial response, n	2(18%)
Very Good Partial Response, n	3(27%)
Progressive Disease, n	6(55%)
DIALYSIS	
Yes, n	1(9%)
No, n	10(91%)
Autologous Stem Cell Transplantation	
Yes, n	2(18%)
No, n	9(82%)
Present status	
Death, n(%)	3 (28%)
Alive, n(%)	8 (72%)

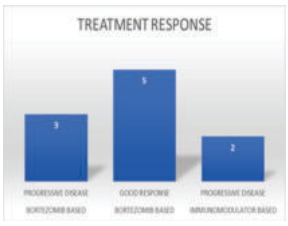

Figure 3

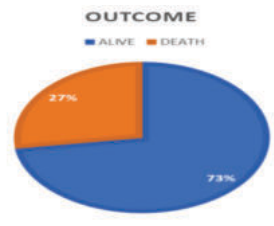

Figure 4

DISCUSSION

AL amyloidosis is a rare progressive and debilitating disease which is caused by the abnormal production of amyloidogenic free light chains by a plasma cell clone [1]. The median age in our study was 54 years-old, different from studies from Japan (65 years), USA (63 years) and Italy (62 Years)[4,5,6]. This is in common with an Indian study (52years) [3], where Indian population will present a decade earlier than western population. The most common organ involved is kidney, which is in common with Chinese study[2] and Japanese study[4], but different from Pavia amyloidosis research and treatment center, which showed heart is the most affected organ[7].

In our study 2(18%) patients had dual organ involvement which is different than Chinese study (68%)[8], south Korean study (65%)[10]and Japanese study (52%)[11]. This may be attributed to early consultation of patients to superspecialists. Badar et al. found that the overall survival of the patients with both cardiac and renal involvement was comparable to that of patients with cardiac involved alone but was worse than that of patients with renal involved alone[9]. In our study, we could not analyse overall survival, but response assessment in our patients with cardiac involvement was poor compared to patients with renal only involvement.

In our study 63% of patients had renal biopsy which is more than a study from Japan (30%)[4]. In our study diagnosis of AL amyloidosis was made using immunohistochemical staining in 63% of patients, compared to 53% in Japanese study[4]. The most common light chain restriction seen in renal biopsy was Lambda in our study which is in consistent with Japanese study[4]. In our study 81% patients received bortezomib based therapy, which is similar to Chinese study (82%)[2], Japanese study (79%)[4]and different from study from USA (95%)[5]. In our study 2(18%) patients had ASCT, similar to 26 % in Chinese study[2], 24% in Japanese study[11] and different from study from USA (54%)[5]. ASCT can induce durable hematological and organ responses in systemic light-chain amyloidosis. However, because of the small number of patients who received ASCT in our study and no long term follow up, we could not analyze this. Out of the two patients with peripheral nerve involvement, one patient died due to disease progression and the other patient is alive but with progressing neuropathic symptoms not responding to treatment. One patient with mediastinal involvement, had a very good hematological response but stable mediastinal mass.

Patients with AL amyloidosis have a poor prognosis, with estimated median survival ranging from 6 months to 18months[8]. In our case series, 3(28%) patients died with median survival of 2.6 years and 8(72%) patients are alive with median follow up of 36 months (IQR-9months- 54 months). This can be attributed to early diagnosis and treatment with bortezomib based therapy and Autologous Stem Cell Transplantation.

CONCLUSION

Our study concludes that early diagnosis and correct treatment are critical in managing patients with AL amyloidosis to achieve a better response and improve survival. A very few centers routinely do ASCT in AL amyloidosis. ASCT should be considered in transplant eligible patients for better survival.

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