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Bence jones Myeloma- An analysis of 28 cases

Oncology

KEYWORDS:

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ABSTRACT

Introduction:
To evaluate the clinical features and response to treatment of light chain myeloma

Back Ground:
Light chain myeloma constitutes 18-20% of multiple myeloma in various series and presents with renal failure in majority of patients.
Material and methods:
We analysed patients with light chain myeloma admitted in our hospital during the period 9/4/04 to 9/2/09. There were a total of 152 patients with multiple myeloma where immunoglobulin levels were available, 103 patients had IgG myeloma, IgA in 19 patients and 2 cases of non secretary myeloma, and twenty eight patients with light chain myeloma.
Results:
There were 28 patients with light chain myeloma 18 males and 10 females (M: F ratio 18:10), age group varying from 35 to 90 years (average 58.2). Fifty percentages of patients had tiredness and 78.5% had bone pain at presentation. Serum creatinine was elevated in 53.5% of patients, anemia in 46% of patients and four patients had high serum calcium levels at presentation. Twenty seven patients presented at stage III Salmon Durie staging system. Sixty four percentage of was kappa chain myeloma and rests were lambda chain myeloma.Twenty three patients were treated with Thalidomide /Dexamethasone and 3 with Vincristine, Adriamycin and Dexamethasone (VAD) and two patients with Melphalan, Prednisolone and Thalidomide (MPT) as initial therapy. Of the 24 evaluable patients 7 patients had complete response (CR), 6 had partial response (PR), 2 had stable disease (SD) and 7 had progressive disease. Two patients died due to disease and four lost follow up.
Conclusions:
Light chain myeloma accounts for 18% of total myeloma cases in our series. More than 50% patients had renal involvement at presentation.54 % patients showed response to treatment.

Introduction

Classic multiple myeloma patients have abnormally increased concentration of M-component which is seen as a spike in gamma region of serum electrophoretic pattern. At the same time, normal synthesis of immunoglobulins is hampered. Hence it gives rise to a profile in which one heavy type of immunoglobulin is increased with a hypogammaglobulinemic background. IgG is the most common immunoglobulin involved with IgA being second most common. The presence of only a light chain monoclonal protein is seen in 20% of multiple myeloma cases and the condition is known as light chain myeloma.[1] Patients light chain myeloma secrete either kappa or lambda light chains. As these chains are low molecular weight molecules, are filtered at glomerulus and reabsorbed and catabolised in renal tubules. If secreted in excessive amount, it can not be reabsorbed fully in the tubules and hence appear in the urine as Bence Jones proteins. These Bence Jones proteins are characterized biochemically by negative dipstick test and positive sulphosalisylic acid test. Heat test for detecting BJ protein is falsely negative in 50% of patients with light chain myeloma

Patients and Methods

All multiple myeloma patients who presented to our institute during the period 9/4/04 to 9/2/09 were analysed. Total numbers of myeloma patients during this period was 250, of which 152 patients had serum immunoglobulins values available. IgG myeloma in 103 patients, IgA in 19 patients, 2 cases of non secretary myeloma and 28 patients with light chain myeloma.

Investigations done on these patients were haemogram, renal function tests, serum albumin, beta2 microglobulin, bone marrow aspiration, skeletal survey, serum immunoglobulin levels and free light chain assay. Immunoglobulin and light chain assay was done by turbidometric method.

Discussion

The most common presenting symptoms of myeloma are fatigue and bone pain.[2] Osteolytic bone lesions and/or compression fractures that can be detected on routine radiographs, magnetic resonance imaging (MRI), or computed tomographic (CT) scans are the hallmark of the disease and cause significant morbidity [3,4,5]. Bone pain may present as an area of persistent pain or migratory bone pain, often in the lower back and pelvis. Pain may be sudden in onset when associated with a pathologic fracture and is often precipitated by movement. Extramedullary expansion of bone lesions may cause nerve root or spinal cord compression. Anemia occurs in 70% of patients at diagnosis and is the primary cause of fatigue. Hypercalcemia is found in one fourth of patients, and the serum creatinine is elevated in almost one half of patients during the course.

An analysis of light chain only myeloma by Cong et al [6] in 42 patients, the main symptoms were fatigue and dizziness (53.5%) and bone pain (58.1%). The main signs were anemia (65 1%) and bone pain (53.5%).In our series 50 % patients had tiredness, bone pain in 78% and 46% patients had anemia at presentation.

In Cong et al study renal function exanimations were performed for 31 patients. Among them, 16 were with stage IIIB and 15 patients with III A. In our study Serum creatinine was elevated in 15 patients. Nine patients had serum creatinine above 3 mg. Pathogenesis of myeloma kidney is attributed to two factors- first is direct tubular toxicity and the second is intratubular cast formation. Direct tubular toxicity involves light chain accumulation inside the cells leading to injury to proximal tubule and loop of Henle. Lambda light chains are found to be more toxic to renal tubules than kappa light chains. These high concentrations may result in cast nephropathy which accounts for around 70% of dialysis dependent renal failure in multiple myeloma patients. Nephropathy reported in different series includes, Winearls, 14 of 20[7], Montseny, 22 of 43(8); Innes, 11 of 14 (9); Magee, 16 of 21(10).Nephropathy increases the morbidity and mortality.

Extended hemodialysis using a high cut-off dialyzer (HCO-HD) removes large quantities of free light chains in patients with multiple myeloma. A study assessed the combination of chemotherapy and HCO-HD on serum free light chain concentrations and renal recovery in patients with myeloma kidney (cast nephropathy) and dialysis-dependent acute renal failure. In dialysis-dependent acute renal failure secondary to myeloma kidney, patients who received uninterrupted chemotherapy and extended HCO-HD had sustained reductions in serum free light chain concentrations and recovered independent renal function [11]

In our study 4/22 had high serum calcium levels at presentation and 27 patients presented at stage III Salmon Durie staging system. Eighteen of our series was kappa chain myeloma and rests were lambda chain myeloma. Cong et al study reported 2 cases of hypercalcemia and 10 cases were kappa light chain, 29 were lambda light chain and 4 were both.

M proteins can be detected by serum protein electrophoresis (SPEP) in 82% of patients with myeloma and by serum immunofixation in 93%. [2] Up to 20% of patients with myeloma lack heavy-chain expression in the M protein and are considered to have light-chain myeloma. The M protein in these patients is always detected in the urine but can be absent in the serum even by immunofixation, making it imperative that protein electrophoresis and immunofixation are always done on both the serum and the urine in all patients in whom myeloma is suspected. Addition of urine protein electrophoresis (UPEP) and urine immunofixation will increase the sensitivity of detecting M proteins in patients with myeloma to 97%. Most (60%) of the remaining patients who are negative for M protein on serum and urine electrophoresis and immunofixation studies will have evidence of clonal paraproteins on the serum free light-chain assay. Currently, only 1% to 2% of patients with myeloma will have no detectable M on any of these tests; these patients have true nonsecretory myeloma [13]

Measurement of the serum free light-chain assay (Freelight, The Binding Site Limited, Birmingham, U.K.) has recently been introduced into clinical practice.[13] This automated nephelometric assay allows quantitation of free kappa and lambda chains (i.e., light chains that are not bound to intact immunoglobulin) secreted by plasma cells. An abnormal kappa/lambda free light-chain ratio indicates an excess of one light-chain type versus the other and is interpreted as a surrogate for clonal expansion based on extensive testing in normal volunteers, and patients with myeloma, amyloidosis and renal dysfunction.[13,14] The assay is performed on automated chemistry analyzers, is widely available, and is commonly used to monitor patients with oligosecretory or nonsecretory myeloma and primary amyloidosis, as well as patients with the light-chain-only form of myeloma.[14,15,16]

The normal serum free kappa level is 3.3 to 19.4 mg/L, and the normal free lambda level is 5.7 to 26.3 mg/L. The normal ratio for free light-chain kappa/lambda is 0.26 to 1.65. The normal reference range in the free light-chain assay reflects a higher serum level of free lambda light chains than would be expected given the usual kappa/lambda ratio of 2 for intact immunoglobulins. This occurs because the renal excretion of free kappa (which exists usually in a monomeric state) is much faster than that of free lambda (which is usually in a dimeric state). [13, 16] Patients with a kappa/lambda free light-chain ratio less than 0.26 are typically defined as having monoclonal lambda free light chain, and those with ratios greater than 1.65 are defined as having a monoclonal kappa free light chain. If the free light-chain ratio is greater than 1.65, kappa is considered to be the "involved" free light chain, and lambda is considered to be the "uninvolved" free light chain, and vice versa if the ratio is less than 0.26.

In a study by Raj Kumar et al, 50 multiple myeloma patients treated with Thalidomide /Dexamethasone showed a response rate of 64%.In that study 6 patients were light chain myeloma and 60% of these patients showed response (17). In our series Twenty three patients were treated with Thalidomide /Dexamethasone and 3 with VAD and others with MPT. Of the twenty four evaluable patients seven patients had CR, six had PR, 2 had SD, 7 had progressive disease, 2 patients died due to disease and four lost follow up. Our study showed over all 54 % response to treatment

Results

Twenty eight patients were diagnosed to have light chain myeloma. Eighteen were males and 10 females (M: F ratio 18:10), age group varying from 35 to 90 years (average 58.2). Major symptoms noted in these patients at diagnosis were tiredness in 14 and bone pain in 22 patients. Thirteen patients had anemia, serum creatinine was elevated in 15 patients and 4 had high serum calcium levels at presentation. Renal biopsy was done in 5 patients, two patients had cast nephropathy. Other three patients had focal glomerulosclerosis and interstitial nephritis. One patient with cast nephropathy needed haemodialysis. Other patients with renal failure were managed conservatively. Eight patients who had renal involvement recovered fully. Four patients showed improvement of renal function with myeloma treatment. Three patients had no marked improvement of renal function with chemotherapy. Twenty seven patients presented at stage III Salmon Durie staging system. Skeletal survey or MRI spine was available in twenty seven patients. Twenty one patients had skeletal changes mostly lytic lesions. Predominant light chain was kappa in 18 rests were lambda chain myeloma. Twenty three patients were treated with Thalidomide /Dexamethasone and 3 with VAD and two patients with MPT. Twenty four patients were evaluable for response. Seven patients had CR, six had PR, two had SD and 7 had progressive disease 2 patients died due to disease and four lost follow up. Eleven responded patients were treated with Thal/Dex chemotherapy and two other patients received VAD.

Conclusions

Light chain myeloma accounts for 18% of total myeloma cases in our series. More than 50% patients had renal involvement at presentation.

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