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DEXAMETHASONE MONOTHERAPY IN A FRAIL AND CHEMOTHERAPY-INELIGIBLE PATIENT WITH END-STAGE MULTIPLE MYELOMA: A CASE REPORT AND LITERATURE REVIEW

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Abstract – *Objective:* *Multiple Myeloma (MM) is increasing in incidence and for the elderly, survival remains poor, mainly due to poor tolerance to chemotherapy which forms an important component of first-line treatment for MM. No previous study has been found on dexamethasone monotherapy for MM treatment.*

Case Presentation: *A 75-year-old female of Chinese descent, previously independent with a background of well-controlled hypertension, type 2 diabetes, hyperlipidemia, and mild Alzheimer's dementia presented to the general practice with fatigue, left groin pain, decreased appetite and dizziness. She was diagnosed with end-stage MM based on serum protein electrophoresis and skeletal survey and treated with only dexamethasone as a chemotherapeutic agent.*

Results: *As of February 2022, two years after the diagnosis of end-stage MM and treatment with dexamethasone monotherapy and supportive therapy, the patient remains adherent to her management plan. She remained alive with mild functional decline and preserved renal function.*

Conclusions: *In addition to managing patients according to the best principles of supportive care, dexamethasone monotherapy may be a good alternative maintenance agent in frail, elderly patients with MM who may not even tolerate attenuated chemotherapy.*

KEYWORDS: *Multiple myeloma, Dexamethasone, Monotherapy, Case report.*

LIST OF ABBREVIATIONS: *AHT - pre-autologous hematopoietic cell transplantation; FISH - immunophenotyping and fluorescence* in situ *hybridization; IVF - intravenous fluid; MM - Multiple Myeloma; PRBC - packed red blood cells.*

INTRODUCTION

Multiple Myeloma (MM) is a hematological malignancy which is characterized by the clonal proliferation of plasma cells. As of 2016, there was close to 140,000 cases of MM diagnosed per year worldwide[1]. Despite increasing incidence of MM in recent years, mortality in countries like the US has fallen by 18% over the past decades with significant advancements in novel MM targeted therapies and transplant protocols[2]. However, improvements in survival were mainly observed in younger patients with such benefits yet to be recognised in the elderly in whom prognosis remains poor[3].

Treatment for MM is complex, especially for the elderly, most of whom are transplant-ineligible. For transplant-ineligible patients, first-line therapy typically involves combination treatment with either daratumumab-lenalidomide, lenalidomide-bortezomib or lenalidomide-dexamethasone followed by maintenance therapy with lenalidomide, with lenalidomide-dexamethasone favoured for frail patients[4]. Unfortunately, even less toxic regimens such as lenalidomide-dexa-

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methasone can be intolerable to elderly patients with up to 30% of patients discontinuing lenalidomide therapy[5,6]. To date, there are no published studies supporting the use of dexamethasone monotherapy in newly-diagnosed MM (7). We present a case of a 75-year-old female with International Staging System (ISS) stage 3 MM treated with dexamethasone monotherapy who remained alive and well 2 years since first diagnosed with MM.

CASE PRESENTATION

A 75-year-old female of Chinese descent, previously independent with a background of well-controlled hypertension, type 2 diabetes, hyperlipidemia, and mild Alzheimer's dementia presented to the general practice with fatigue and left groin pain in January 2020. In addition, patient complained of decreased appetite and dizziness which she has experienced over the past 3 months. There were no reports of sensation abnormalities. Systems review was otherwise unremarkable. Her medications included rosuvastatin 5 mg OD, metformin 1000 mg BD, sitagliptin 50 mg BD, irbesartan 150 mg OD and donepezil 5 mg. The patient was previously active and independent and engaged in Tai-Chi daily.

Investigations revealed a hemoglobin of 6.4g/dL, platelet count of 131x10^3/µL, leucocyte of 3.3 x10^3 /µL with monocyte predominance, ESR of 162 mm/hour, serum calcium of 9.2 mg/dL, serum creatinine of 3.16 mg/dL, eGFR 14 and normal liver function test. Urinalysis was positive for albumin and blood. Patient was admitted to the hospital for transfusion of packed red blood cells (PRBC), supportive treatment with intravenous fluid (IVF) and analgesia and workup for investigation of pancytopenia and renal failure. Considering her renal failure, irbesartan was switched to nifedipine, metformin and sitagliptin were switched to gliquidone and linagliptin. The patient was discharged two days later and followed up in the outpatient hematology clinic.

Serum protein electrophoresis (Figure 1) and serum immunofixation electrophoresis (Figure 2) were conducted. Skeletal survey revealed multiple lytic lesions in the skull and the left inferior pubic ramus. As the patient refused bone marrow biopsy, immunophenotyping and fluorescence *in situ* hybridization (FISH) for disease prognostication was not possible.

A diagnosis of MM was made, and patient was commenced on treatment with oral lenalidomide 15 mg on alternate days (every 48 hours) and oral dexamethasone 20 mg on days 1, 8, 15 and 22 of a 28-day cycle, aspirin 100 mg daily for thromboprophylaxis and monthly ibandronate infusion. Four weeks after commencing combination therapy of lenalidomide and dexamethasone, patient presented to hospital with significant lethargy and breathlessness. Hemoglobin, platelet, and leucocyte count were found to be 6.2g/dL, 94x10^3/µL and 1.9x10^3/µL, respectively. A diagnosis of lenalidomide-induced pancytopenia was made. Lenalidomide was discontinued and patient received PRBC transfusion.

Following this admission, the patient and the family opted to cease lenalidomide treatment indefinitely and a shared decision between the

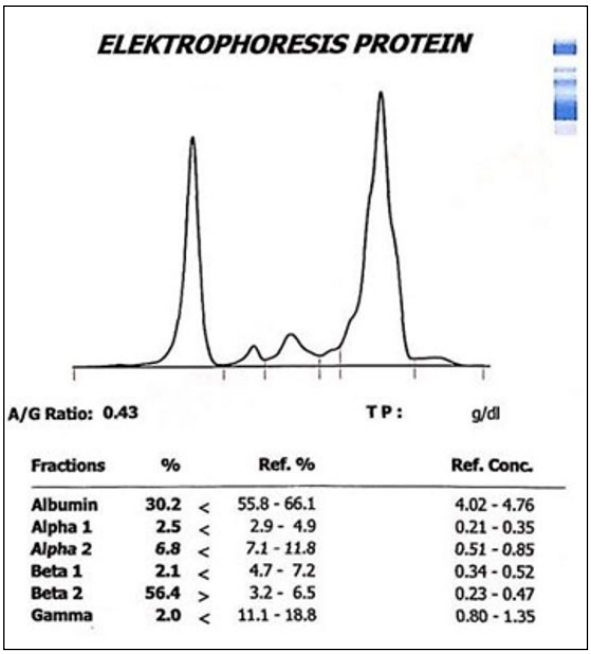

Fig. 1. Serum protein electrophoresis (SPEP) of the patient. Serum free light chain Kappa and Lambda were 32.1 mg/L and 3751.0 mg/L respectively, with a ratio of lambda:kappa of 117.

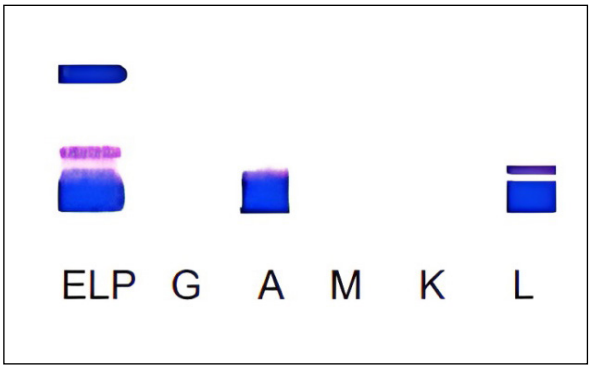

Fig. 2. Serum immunofixation electrophoresis (IFE) with agarose gel of the patient. Serum immunofixation revealed a monoclonal gammopathy of IgA lambda (IgA: 4,236 mg/dL). Beta2-microglobulin was significantly raised at 16.06 mg/L.

hematologist, nephrologist and the patient was made to continue dexamethasone monotherapy at a dose of 6 mg thrice weekly with twice weekly recombinant human erythropoietin injection, monthly ibandronate infusion, and to continue her medication plan for her other comorbidities and perform full blood counts every fortnight, with a plan of PRBC transfusion if her hemoglobin falls below 80 or symptomatic for anemia. The patient refused monitoring of the progression of the MM and palliative care team involvement.

RESULTS

As of February 2022, two years after the diagnosis of end-stage MM and treatment with dexamethasone monotherapy and supportive therapy, the patient remains compliant with her management plan. She remained alive with mild functional decline and preserved renal function (eGFR: 13).

DISCUSSION

Literature on previous dexamethasone laboratory studies and in patients prescribed dexamethasone monotherapy for pre-stem cell transplant induction therapy provided insight into possible mechanisms supporting the continued survival of the patient in this case beyond the 6 months median survival of untreated end-stage MM[8]. Kumar et al[9] demonstrated that the overall response rate for MM patients treated with dexamethasone was 74% as compared to 86% in a second group of patients treated with the combination of vincristine, doxorubicin, dexamethasone as a pre-autologous hematopoietic cell transplantation (AHT) induction therapy. This highlighted the efficacy of dexamethasone as an induction agent in MM. Previous laboratory studies have also shown that dexamethasone induced apoptosis of myeloma cells in various ways including but not limited to, induction of the proapoptotic proteins, transactivation through the glucocorticoid response element, transrepression of Nuclear factor kappa B, phosphorylation of and activation of related adhesion focal tyrosine kinase[10-12].

Elderly patients are more vulnerable to the adverse effects of chemotherapy and targeted therapy. Consequently, elderly patients are not eligible for the novel MM therapeutic agents including AHT. Unfortunately, even for current agents recommended in frail patients with MM such as lenalidomide and bortezomib, adverse effects are observed in up to 30%, with a significant proportion eventually discontinuing therapy[5,6]. There is a need for new therapeutic agents and regimens for maintenance therapy in this group of patients with MM. We showed that for the first-time dexamethasone monotherapy may be a potential viable candidate to fill this current gap.

CONCLUSIONS

The management of MM in elderly, frail patients remain extremely challenging. In addition to managing patients according to the best principles of supportive care, dexamethasone monotherapy may be a good alternative maintenance agent in frail, elderly patients with MM who may not even tolerate attenuated chemotherapy. Future studies are warranted to confirm the results of this study.

Ethics approval and consent to participate:
Not applicable

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Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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OR contributed to manuscript writing, figure preparation and formatting. YL was a contributor to manuscript writing and formatting. All authors read and approved the final manuscript.

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