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A RARE CASE OF LIGHT CHAIN DISEASE WITH PURE RED CELL APLASIA AND EFFECT OF PULSE HIGH DOSE DEXAMETHASONE

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Abstract

Anemia is a common finding in patients with multiple myeloma (MM) and is usually contributed by marrow infiltration, renal impairment and systemic illnesses. Pure red cell aplasia (PRCA) however, has only rarely been reported in patients with multiple myeloma (MM), with only a few case reports documented in the literature. In this case report, we present a unique case of PRCA associated with kappa light chain disease of MM. The patient was successfully treated with pulse high dose dexamethasone with bortezomib with dose modification and blood transfusion being avoided further.

INTRODUCTION

Anemia in multiple myeloma (MM) is a common complication in patients and is a problem in more than two thirds of all patients. Some of the important factors contributing to anemia in MM patients are: anemia of chronic disease (ACD), relative erythropoietin (EPO) deficiency and myelosuppressive effects of chemotherapy (Ludwig H et al, 2004). Pure red cell aplasia (PRCA) however, has only rarely been reported in patients with MM, with only a few case reports documented in the literature (Orchard J et al, 1997). Light chain disease (LCD), a variant of MM, comprises about 18% of MM patients in which the malignant plasma cells produce free monoclonal light chains but no associated heavy chain or complete immunoglobulin. In this case report, we present a unique case of PRCA associated with kappa LCD successfully treated with pulse high dose dexamethasone with bortezomib, a proteasome inhibitor.

CASE REPORT

An 80 year old male patient presented with weakness, pallor, vertigo, and low back pain for four months. Patient had no history of fever or bleeding from any site. He had received four units of packed red blood cell (PRBC) transfusions and an analgesic. He had no significant personal and family history of this condition. The patient had co-morbidities including type 2 diabetes mellitus, ischemic heart disease, hypertension, left leg varicose vein, and osteoarthritis of left knee joint at the time of this report. His regular medications included antianginal, antihypertensive, and oral hypoglycemic drugs.

On examination the patient had severe pallor without icterus, hepatosplenomegally, lymphadenopathy, and neuropathy. The laboratory reports included hemoglobin (Hb) 37 g/L, total leukocyte count 12.2 x 10^9/L, differential neutrophils 77%, lymphocytes 11%, monocytes 0.4%, eosinophil 0.8%, basophil 0.0%, platelet count 119 x 109/L, erythrocyte sedimentation rate (ESR) 155 mm in first hour, mean corpuscular volume (MCV) 101.6 fl, mean corpuscular haemoglobin (MCH) 31.4 pg. Red Blood Cells (RBCs) were predominantly normocytic, normochromic.

Corrected reticulocyte count was 0.5% and direct Coomb's test was negative. His fasting plasma glucose was 6 mmol/L, urea 5 mmol/L, creatinine 88.3 µmol/L, serum calcium 2.2 mmol/L, total bilirubin 6.8 mmol/L, total protein 55g/L, albumin 34g/L, globulin 21g/L, SGOT 0.25 µkat/L, SGPT 0.27 µkat/L.

Serum and urine protein electrophoresis revealed a faint 'M' band (SPE: 2% ~ 1.1 g/L) in the gamma region (Immunofixation revealed IgG kappa). Serum beta 2 micro globulin was 2500 mcg/L, serum free light chain assay showed kappa 42.08 mg/L, lambda 13.11 mg/L, free light chain (FLC) ratio was 03.21. X-ray spine showed lytic lesions in the L3 & L4 vertebrae with compression fracture (figure 1A). Straight X-ray skull shows few tiny lytic lesions (figure 1B). X-rays of chest and other long bones are normal.

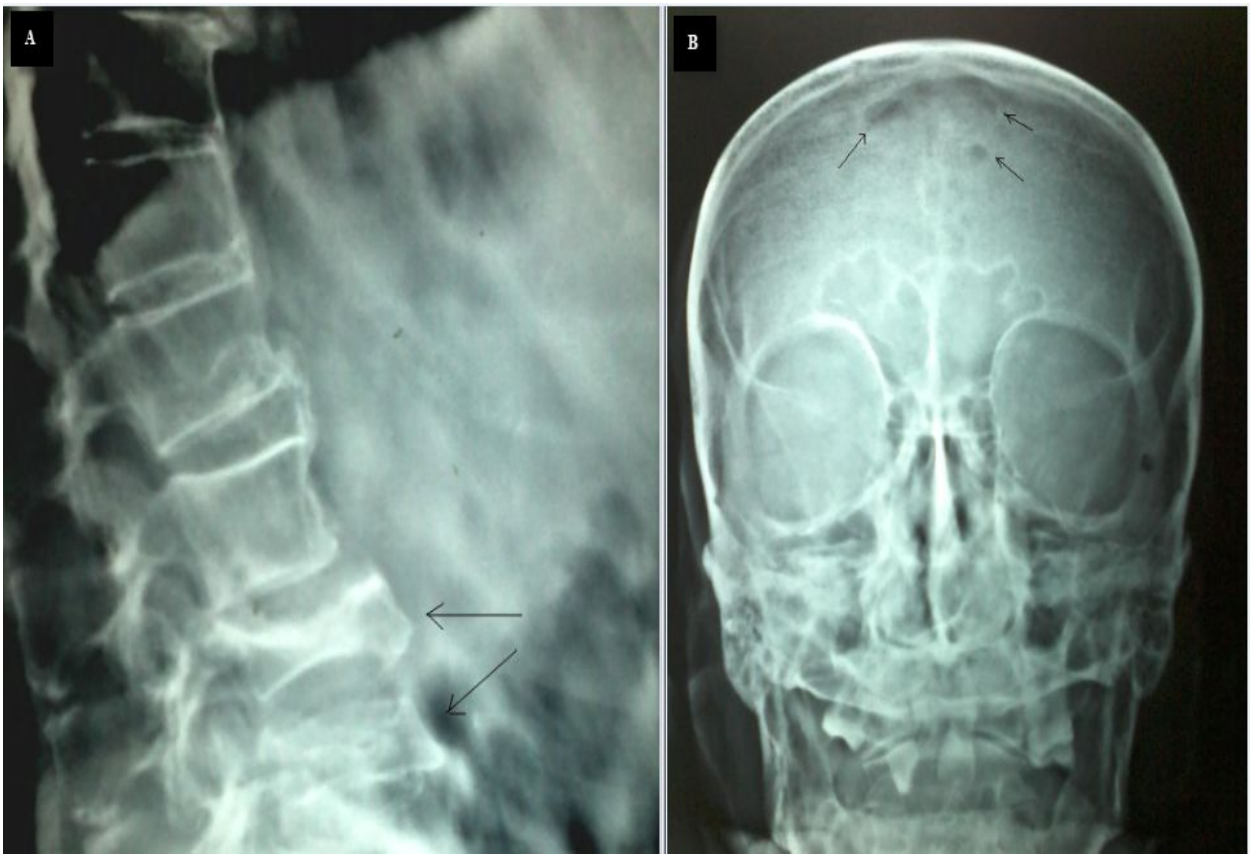

Figure 1: Straight X-Ray of spine (A) show lytic lesions in the L3 & L4 vertebrae with compression fracture (arrow) and skull (B) showing tiny lytic lesions (arrow)

Bone marrow aspiration (figure 2A) was cellular with severely depressed erythropoiesis (<1%) and normal myelopoiesis and megakaryopoiesis. Plasma cells increased (14%) and many atypical forms were observed. Iron store was adequate. Thus, gave an impression of plasma cell dyscrasia with PRCA. Bone marrow biopsy revealed cellular marrow with severely depressed erythropoiesis and increased interstitial plasma cell infiltration (figure 2B).

Ultrasonography of whole abdomen was within normal limits and stool for occult blood test was negative. Parvo-virus B19 DNA assay done with PCR was negative. Patient was treated initially with bortezomib 1 mg/m^2 at 1, 8, 15, and 22 days in a total of 35 day cycle and 10 mg dexamethasone (age and co-morbidity adjusted dose) once a week (Zweegman S et al, 2014). Starting from the middle of the second cycle, dexamethasone dose was increased to 20 mg. After this, hemoglobin was maintained in the range of 6-65 g/L without blood transfusion but no further increment of hemoglobin level. Starting from the middle of third cycle, dexamethasone at a dose of 20 mg (age

adjusted dose) was given for four consecutive days (pulse dexa). Hemoglobin increased to 88 g/L after 2 weeks and 100 g/L after 4 weeks and from fourth cycle onwards the patient received 20 mg dexamethasone once a week (figure 3). After 6 cycles of therapy, the patient maintained 100g/L without any blood transfusion and patient was in complete remission.

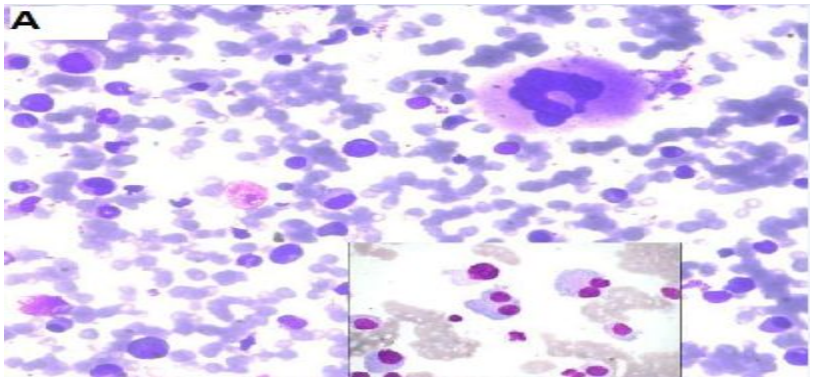

Figure 2: (A) bone marrow smear, Leishman stain, 40 x magnification (inset: oil immersion) was cellular with severely depressed erythropoiesis (<1%) and normal myelopoiesis and megakaryopoiesis. Plasma cells increased (14%) and many atypical forms were observed

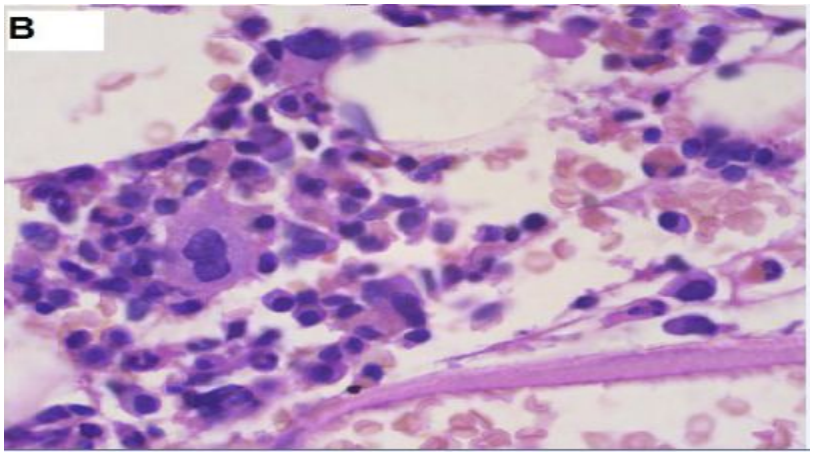

Figure 2(B) Trephine biopsy (H & E stain)- revealed cellular marrow with severely depressed erythropoiesis and increased interstitial plasma cell infiltration.

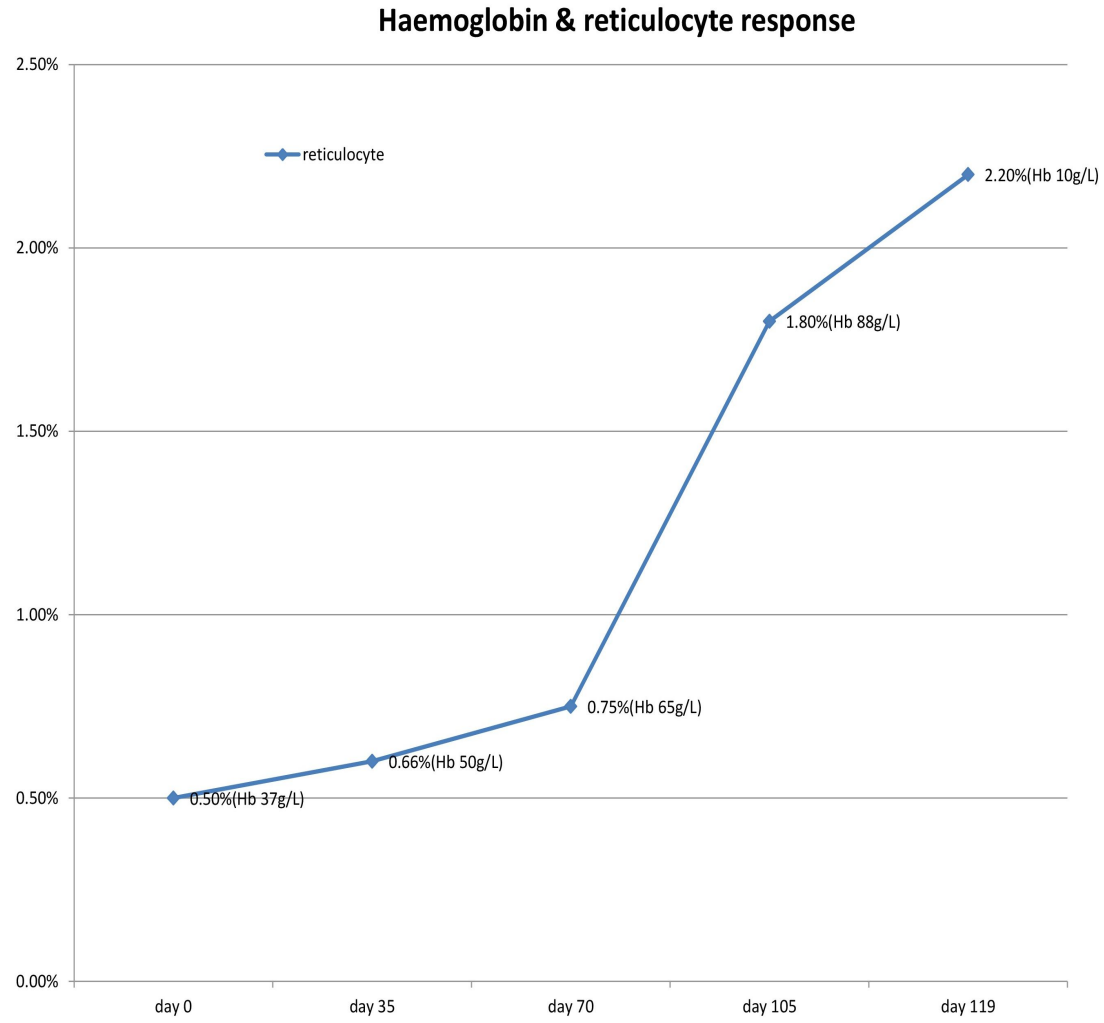

Figure 3: Hemoglobin and reticulocyte response measured over a period of 4 months.

DISCUSSION

Acquired PRCA has infrequently been reported in association with paraproteins. Resegotti *et al* (1978) discovered six cases prior to 1978. Few reports are there in the Japanese literature that PRCA may be associated with antibodies that inhibit erythropoiesis (Masauzi N et al, 1993), with cytotoxic T cells that suppress red cell production or with persistent parvovirus infection (Karmockine M et al, 1995). All of these mechanisms have been reported in patients with monoclonal gammopathies. Orchard J *et al* (1997) showed cases treated with VAD (vincristine 0.4 mg daily for 4 days by continuous infusion, doxorubicin 9 mg/m^2 daily for 4 days by continuous infusion and dexamethasone 40 mg/d for 4 days). After the second course there was a transient reticulocytosis peaking at 334 x 10^9/l associated with 10% normoblasts in the bone marrow smears and persisting for 10 days.

Sarathy KS *et al* (2013) also reported two cases, one PRCA with LCD and another PRCA with MGUS. In both cases, patients responded well with bortezomib therapy. They treated the case of LCD with PRCA treated with bortezomib that induced long lasting remission of myeloma and resulted in reversal of PRCA and hence transfusion independence. The second case responded with combination of prednisolone and oral cyclophosphamide. Deotare

UR *et al* (2006) showed Pulse dexamethasone is successful in PRCA following post-transplant cases. Pulsed oral high dose dexamethasone has also been found to improve pure red cell anemia after major ABO-mismatched hematopoietic stem cell transplantation (Sharma SK et al, 2015). But our case is unique in a sense that high dose pulse dexamethasone is highly effective in the combination of LCD and PRCA for rapid response specially to avoid repeated blood transfusion and is a low cost therapeutic option indeed.

CONCLUSION

Pure red cell anemia is a challenge in kappa light chain diseases of MM patients. A treatment with low dose dexamethasone might have an insufficient response at the beginning but the associated boost in reticulocytosis with increment of haemoglobin after treatment with high dose pulse dexamethasone can be a good therapeutic option in this group of patients. The hematological response of pulse high dose dexamethasone therapy can also avoid blood transfusion in selected MM patients. However; more case series and larger randomized trials are required to further substantiate this finding.

CONFLICT OF INTEREST

NONE

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