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Case Study

Primary Plasma Cell Leukaemia

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ABSTRACT

Plasma cell leukemia (PCL) is a rare form of malignant plasma cell dyscrasia. It can occur as a primary form without prior evidence of multiple myeloma or as a secondary form which is a terminal event in multiple myeloma. It is characterised by a proliferation of plasma cells in blood and the bone marrow. The outcome of plasma cell leukemia is poor with conventional therapy. Here we illustrate a case of primary plasma cell leukemia complicated by paraplegia. The patient initially responded to combination chemotherapy but succumbed to the disease two months after presentation.

Keywords: Clinico-pathological features, management, plasma cell leukaemia

INTRODUCTION

Plasma cell leukemia (PCL) which is the leukemic variant of multiple myeloma is a rare disorder.[1,2] It represents 2% of plasma cell dyscrasia.[3,] The diagnosis is based on presence of more than 20% plasma cells in the peripheral blood or absolute count of plasma cells of more than 2 x 10^9 /l.[3] Primary PCL is termed when the patient is first diagnosed in the leukaemic phase. Secondary PCL is the transformation of previously recognised multiple myeloma. Clinical characteristics are almost similar in both.

This aggressive variant of plasma cell dyscrasia usually affects patients in their 6^{th} decade.[4] Rarely does this illness occur in young age groups.[5,6] The primary form is more aggressive but responds better to treatment as compared to the secondary form. Survival with standard combination chemotherapy is very poor. We report a case of primary plasma cell leukemia in a 53-year-old man initially presented with paraparesis which progressively worsened to paraplegia. The literature on the clinical features and management approaches for this rare, aggressive entity is reviewed.

THE CASE

A 53-year-old man was referred for further management of paraparesis which progressively worsened to paraplegia of both lower limbs within one month duration. This was associated

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with other neurological symptoms such as back pain, incontinence and numbness of the lower limbs.

Physical examination revealed multiple subcutaneous soft tissue masses over the left supraorbital, paraspinal and right scapular region with sizes ranging from 1.5 to 12 cm in diameter. His liver was enlarged. Neurological examination of both lower limbs showed normal tone, power of 0/5 and hyporeflexia of the knee and ankle jerks. There was loss of sensation at T4 level and below. The anal tone was lax with loss of peri-anal sensation.

Initial investigation revealed hemoglobin of 13 g/dl, white blood cell (WBC) of 22.9 x 10^9/l and platelet of 154 x 10^9/l. Smear of his peripheral blood showed leucoerythroblastic picture, rouleaux formation of red blood cell (RBC) and presence of 69% of atypical lymphoid cells (plasmacytoid in appearance)(Figure 1). Serological assessment showed the following results: ESR of 18 mm/hour; calcium of 2.91mmol/l and LDH of more than 4000 u/l. Bone marrow revealed infiltration with 60% plasma cells/plasmablasts. These cells were positive for CD79, CD38, and cytoplasmic lambda light chain. Serum protein electrophoresis (SPE) and immuno-fixation studies showed immunoglobulin G (IgG)ë paraprotein at a concentration of 21.4g/l. Free lambda light chain was detected in the urine.

Magnetic resonance imaging (MRI) revealed multiple spinal metastases with paraspinal masses at the T4/T5 and T6/T7 levels ranging from 3 to 6 cm in diameter (Figure 2). These masses had extended to the spinal canal, causing narrowing of the spinal cord. Multiple lytic lesions at the left seventh rib, ileum and ischium were also seen. MRI of the thorax and abdomen (Figure 3) showed a huge mass at the left seventh rib, measuring about 5 x 6 cm in diameter. The skin biopsy specimen showed intense infiltrates of these similar cells in the bone marrow. Chromosomal studies showed complex chromosomal abnormalities with a few hyperdiploidies.

Primary PCL was diagnosed. He responded well to the first cycle of combination chemotherapy: Vincristine 0.4mg/m^2, Doxorubicin 9 mg/m^2 and Dexamethasone 40 mg. Clinically, the masses were significantlly reduced in size. His neurological symptoms and general health status also improved. The patient was on course for a few cycles of monthly combination chemotherapy (VAD). Unfortunately he developed septicemia and succumbed to his illness three weeks after the first chemotherapy, two months after presentation.

DISCUSSION

Plasma cell leukemia is a rare entity with an incidence of less than one case per million population.[2] In Malaysia particularly, this is the first case report. Primary plasma cell leukemia is more aggressive than the secondary form. The median interval from onset of symptoms to diagnosis is approximately 3 months and 16 months respectively.[3]

Typical symptoms as in multiple myeloma are the common features in PCL. Clinical aggressiveness of the disease can be assessed by the extra-osseous manifestations of the disease.[1,10] Involvement of the spleen, liver and skin nodules is frequent in PCL.[4] In this rare case, our patient had paraparesis which worsened to paralysis of the lower limbs within a month of presentation as complication of the spinal canal infiltration by paravertebra masses. Other rare sites of organ involvement are kidney, heart, pleura, testes, skeletal muscle and the central nervous system.[4]

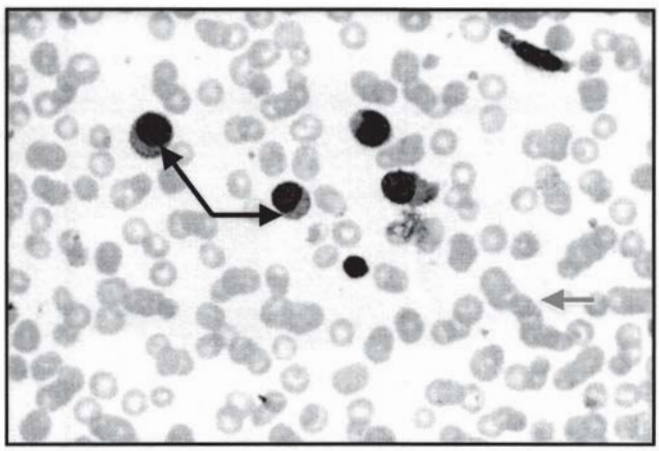

Figure 1. Peripheral blood smear showing rouleaux formation (grey arrow) of RBC and circulating plasma cells with classical eccentric nuclei, paranuclear hof and abundant basophilic cytoplasm (black arrow). Wright –stain X 400

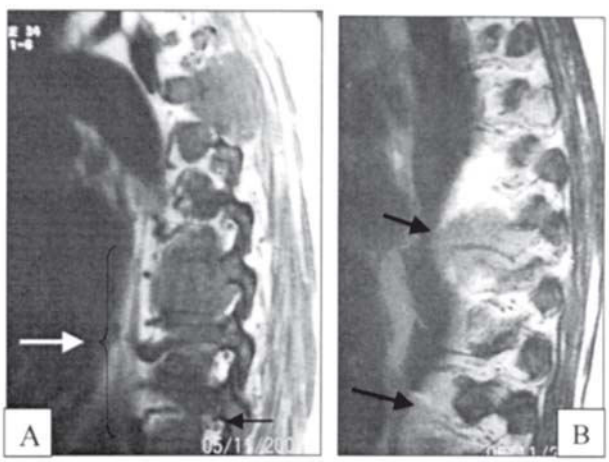

Figure 2. A : MRI of the thoracolumbar region showed multiple lytic lesions of T(4 -7) (white arrow) and 7th posterior rib (black arrow); B: MRI revealed para spinal masses at the T4/T5 and T6/T7

Laboratory haematological abnormalities are encountered in most PCL cases. Anaemia with hemoglobin of less than 8.5 g/dl and thrombocytopaenia of less than $100x10^9$/l are seen in 50% of cases.[4] In contrast, both parameters were within reference range [4,6,7] as in our case. Diagnosis of PCL is characterised by presence of circulating peripheral blood plasma cell exceeding > 20% or 2 x 10^9/l of the white blood cell (WBC). Seventy- five percent of

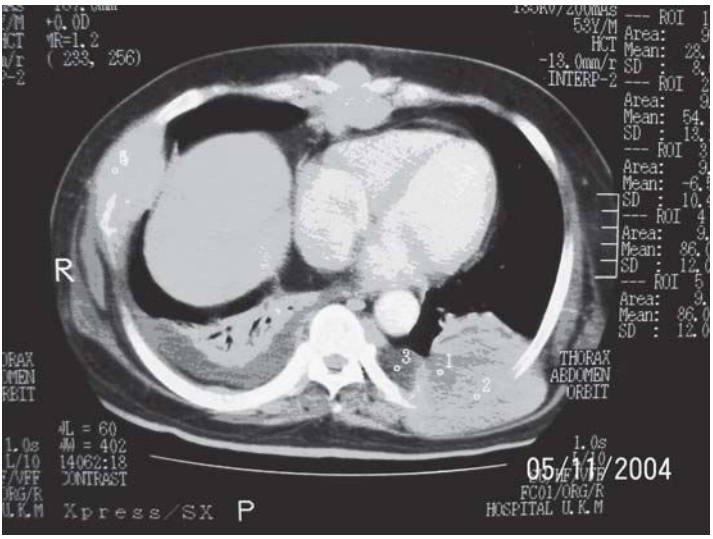

Figure 3. MRI showing huge mass at the left seventh rib

cases with primary PCL had WBC count of > 10x 10^9/l, as observed in this patient.[4,6,7] Pancytopaenia is rarely a feature. [4]

Bone marrow (BM) plasmacytosis varies between reported cases. The majority have BM plasmacytosis of more than 20% of the total nucleated cells.[4] These cells are positive for HLA-DR and CD38 but are negative for CD20. The B-cell associated antigens usually are negative in all patients with PCL whereas early B-cell antigen (CD19 and CD20) are present in only a few of the reported cases.[4] Lytic lesions is one of the criteria for a diagnosis of plasma cell dyscrasia. Extensive lytic lesions as observed in this case are less frequently seen in primary PCL as compared to non-leukemic phase myeloma.[5,10]

Demonstration and quantification of monoclonal immunoglobulin is one of the criteria in diagnosing plasma cell dyscrasia. IgE and IgDê with κ isotopes are frequently found in PCL.[2,3] In contrast, our case had IgGë type paraprotein. Bence–Jones proteinuria, as demostrated in this patient, is found in approximately 80% of cases.[4] Similar to multiple myeloma, the few reported cases were the non-secretory type.[4]

Serological assessment for other biological parameters such as serum calcium, liver function test, renal profile, serum beta-2-microglobulin and serum LDH level are important prognostic factors as in multiple myeloma.[3,4,5] A beta-2-microglobulin of more than 6 mg/L is a common finding in PCL. As in this case, diploid and hypodiploid karyotypes are the common complex cytogenetic abnormalities found in PCL.[1,2,4,8]

The optimal treatment for PCL is not well defined. As it is also recognised as stage II-III multiple myeloma, the treatment approach consists of combination chemotherapy with or without stem cell transplant. Noel and Kyle[2] reported that about 54% of patients achieved partial response to melphalan and prednisolone regime with median survival of about a year. In contrast, Dimopoulos *et al.*[1] reported that none of his 10 patients responded to a

similar approach and their survival was only 2 months. Patients who were treated with more intensive treatment consisting of VAD or cyclophosphamide and etoposide had a response rate of 59% with a median survival span of 20 months.[1] A modified form of VAD regimen (using liposomal Doxorubicin to reduce cardiotoxicity) also seems to work in PCL.[9]

Therapies using high dose chemotherapy followed by autologous bone marrow or stem cell support have been encouraging. Hovenga *et al*.[7] reported two of three cases were in complete remission for almost two years after receiving combination chemotherapy followed by autologous peripheral blood stem cell (PBSC) transplant. Sica *et al*.[11] reported a case with complete remission for more than 2 years after being treated with a similar approach. The experience with allogeneic stem cell transplantation in PCL is even more limited.

Combination chemotherapy consisting of bortezomib, cyclophosphamide and dexamethasone is a current approach with a promising outcome. Granssinger *et al*. [12] and Seok *et al*. [13] reported rapid and effective response with the commencement of this regimen. This approach deserves consideration and further study in a larger group of patients.

CONCLUSION

In summary, the presentations and clinicopathologal findings of PCL mimics the presentation of acute leukaemia. Prognosis of PCL is poor. More effective therapeutic approaches need to be established.

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