Non-secretory Primary Plasma Cell Leukemia – A Case Report

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Abstract Plasma cell leukemia (PCL) is a rare disease and the least common variant of multiple myeloma. It accounts for 2-3% of all plasma cell dyscrasias with poor prognosis. We report a 65 year old Sudanese lady presented to oncology clinic with complaint of inability to walk for 2 weeks. Laboratory findings showed anemia, thrombocytopenia and white blood cell count of 49.4×10^9/L, 62% of which were plasma cells. Bone marrow aspirate showed infiltration by 75% plasma cells some with abnormal forms, Immunophenotyping revealed plasma cell population which were CD38 and CD138 positive, surface, cytoplasmic kappa and lambda were negative. Plasma protein electrophoresis was normal denoting it as non-secretory plasma cell leukemia. Unfortunately the patient passed away before doing further investigations or receiving any treatment.

Keywords: Non-secretory, plasma cell, leukemia

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1. Introduction

Plasma cell leukemia (PCL) is a rare, yet aggressive plasma cell (PC) neoplasm. It is a variant of multiple myeloma (MM). PCL can either originates de novo primary PCL (Ppcl) or as a secondary leukemic transformation of MM (secondary PCL) [1]. Clinical distinctions that have been reported between the two forms of multiple myeloma include a younger age, a higher prevalence of hepatosplenomegaly, lymphadenopathy, thrombocytopenia, a lower serum M protein level, extramedullary involvement, and renal failure when leukemia is present [2]. An interesting feature of pPCL is that the majority of these individuals do not have clinical evidence of overt bone destruction. Osteolytic lesions are more common in secondary PCL (sPCL) as they are also more common in pre-existing MM (sPCL 53% vs. pPCL 18%) [3].

The diagnostic evaluation of a patient with suspected PCL should include a review of the peripheral blood smear, bone marrow aspiration and biopsy, serum protein electrophoresis (SPEP) with immunofixation, and protein electrophoresis of an aliquot from a 24 h urine collection (UPEP) [1] The diagnosis requires that: (i) for a blood leukocyte count exceeding 10×10^9/L, at least 2×10^9/L are circulating plasma cells, or (ii) for a peripheral blood leukocyte count below 10×10^9/L, at least 20% of the circulating cells must be plasma cells [4]. Immunophenotyping reveals differences between MM and

PCL, CD38 and CD138 antigen expression are excellent PC markers and does not differ between MM and PCL, while CD2, CD3 and CD16 are consistently negative. The frequency of CD10+, CD13+ and CD15+ is similar in both groups. Nevertheless significant differences were observed for the expression of CD20, CD56, CD9, CD117 and HLA-DR antigens showing there is some overlap in antigen expression from the pattern for MM. The CD20 antigen displayed higher reactivity in PCL, whereas the other four, including the CD56 (NCAM) antigen, have a lower expression. Negative expression of CD56 has been associated with extramedullary MM [5]. The prognosis of patients with plasma cell leukemia treated with conventional therapy has been reported with median survivals of 7 to 14 months for those with primary plasma cell leukemia and 2 to 7 months for those with secondary plasma cell leukemia [6].

2. Case report

A 65 year old Sudanese lady presented to oncology clinic in August 2012 with a complaint of inability to walk and vomiting for 2 weeks. Physical examination showed pallor, hepatomegaly, spleen and lymph nodes were not palpable.

The initial laboratory results were as follow: hemoglobin 8.2 g/dl, white blood cell count 49.4×10^9/L, a differential of 62% plasma cells and 17% lymphoplasmacytic cells, with an absolute plasma cell

count of 30.6×10^9/L and platelets count 32×10^9/L. Accordingly a provisional diagnosis of PCL was stated. Plasma cells were found to constitute 75% of the bone marrow nucleated cells when examining the bone marrow aspirate some of them had abnormal forms (binuclearity or multinuclearity) but the trephine biopsy was inadequate for interpretation [Figure 1]. Immunophenotyping using Beckman Coulter flowcytometer revealed a population constituting 68% of the cells and expressing CD45, CD38, CD138, and lacking HLA-DR, CD 19, CD20, CD22, surface and cytoplasmic kappa and lambda expression. Plasma protein electrophoresis was done and showed normal pattern, so the case was diagnosed as non-secretory primary PCL [Figure 2].
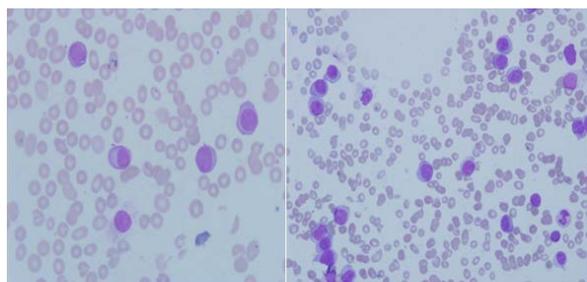
Figure 1. Blood film(A) and bone marrow aspirate (B); showing plasma cells and lymphoplasmacytic cells with rouleaux formation
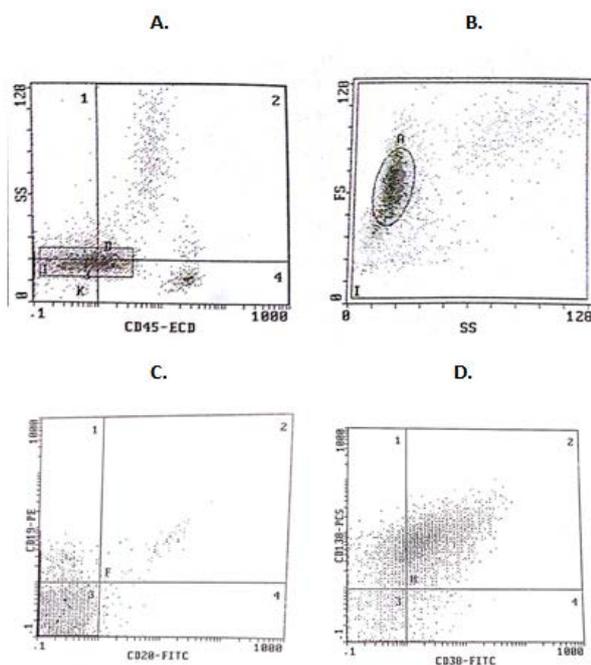
Figure 2. Flowcytometry of venous sample of the patient. A. Dot plot scatter showing population having moderate side scatter and high forward scatter constituting 67%. B. CD45 scatter showing 57% population that are weakly positive to negative. C. These cells are negative for both CD19 and CD20. D. and coexpressing both CD38 and CD138 (57%)

No further investigations were done and the patient didn't receive any treatment because she died few days following initial presentation to hospital.

3. Discussion

Patients with PCL represent a unique subset of patients with multiple myeloma. From 1960 through 2008, of 6974 new patients with multiple myeloma seen at Mayo clinic, 90 fulfilled the criteria for having PCL (1.3%). In an analysis of the Surveillance, Epidemiology, and End Results (SEER) database, there were 49,106 patients with multiple myeloma; 291 had PCL (0.5%) [7]. Rarity of PCL can be assessed from the fact that at M.D. Anderson Cancer Center, 27 patients with PCL were seen in a 20 years period whereas at Policlinico San Matteo in Italy, 15 cases were seen in 15 years both representing 2-5% of total cases of multiple myeloma seen at these centers [8,9].

Our patient was the first patient to be diagnosed as PCL in the hospital since its establishment in 2000 in what denoting the rarity of this diagnosis. The death of the patient soon after presentation emphasized how aggressive this disease is. The original diagnostic criteria of PCL were established in 1974 by Noel and Kyle, requiring both more than 20% circulating plasma cells and an absolute count greater than 2×10^9/l plasma cells in peripheral blood, these two criteria are fulfilled in this case These criteria have not been evaluated prospectively to determine if a need for any modification is required [10]. Plasma cells in PCL frequently display a more immature phenotype. Expression of pan-B cell antigen CD20 has been shown in 50% of PCL cases compared to 17% of multiple myeloma cases [11], which was negative in our patient. Moreover; Garcia-Sanz *et al* reported that CD20 expression has been associated with shorter survival [5]. HLA-DR is observed to have lower expression in PCL than in MM which was negative here.

In approximately 20% of MM cases, the paraprotein consists of free light chains only and may not be associated with a paraprotein spike on serum electrophoretic studies [12] SPE is the main screening tool for the assessment of intact monoclonal immunoglobulins, while serum immunofixation electrophoresis is more sensitive for light chain detection. One of the problems with measurement of urinary light chains is that dipstick tests for detecting proteinuria are unreliable in recognizing free lightchains [13], our reported case was mainly diagnosed by morphology then by flowcytometry other tests were not done because the patient died soon after presenting to the hematology department.

Overall, incidence of PCL is less than 1 case per million populations [14]. This is the reason for lack of prospective data on treatment regimens and treatment outcome in large trials in this disease.

Takahashi *et al* reported two cases one of them was an 85 year old male diagnosed as nonsecretory PCL that had no M-band by serum electrophoresis and no monoclonal protein by serum and urine immunofixation but the number of peripheral plasma cells gradually increased, and the patient died due to the disease progression before starting chemotherapy as what happened to our reported case. Their second case was a 78 year woman presented with Compression fractures of thoracic and lumbar vertebrae, The white cell count was 11,900/μL and 20% of the differential count was reported as atypical cells and were found to be plasma cells and Urinary protein was negative. The serum protein electrophoresis showed no M-spikes, while serum and urine immunofixation electrophoresis demonstrated no monoclonal proteins. Therefore, a diagnosis of primary nonsecretory PCL was made and the patient was successfully treated with bortezomib-containing chemotherapy [15].

Agarwal and colleagues reported 10 cases of PCL, their finding were: Leukocytosis (mean; 53.3 × 109/L, range; 21-88 × 109/L), and anemia (mean; 68 g/L, range of hemoglobin; 58-84 g/L), were seen in all cases. Thrombocytopenia (mean; 64.1 × 109/L, range of platelets; 29-125 × 109/L) was seen in nine cases. In one case platelet count was normal. On manual differential count in PB smear, the plasma cells percentage were more than 20% (range; 22-95%) in all cases except one case (14%), in which an absolute count of the plasma cells was >2000 cell/µl biochemical investigations revealed hypercalcemia (67%), high serum creatinine (70%) and high blood urea levels. They tested the blood of the patients and diagnosed the PCL by flowcytometry and they concluded that flow cytometry is useful to differentiate PCL from other chronic lymph proliferative disorders with plasmacytoidmorphology as well as from non-neoplastic reactive plasma cells [16].

Response to treatment of PCL is poor with a median survival which is less than 1 year, primary PCL requires aggressive management (intensification of high dose chemotherapy followed by allogenic/autologous stem cell) so as to provide any survival advantage [17]. When autologous stem cell transplantation (ASCT) is done, patients with multiple myeloma (MM) have their tumor burden reassessed approximately 100 days later [18], Gonsalves et al reviewed the outcomes of 430MM patients who underwent their first ASCT at the Mayo Clinic, Rochester, within 12 months of their diagnosis between 1999 and 2012; moreover, none of them achieved a complete remission (CR) at day 100. One-hundred sixty-seven (39%) of those patients had a continued response at a median of 9.4 months post-ASCT compared with the 263 (61%) patients who did not have a continued response and their study suggested that in MM patients undergoing ASCT, a continued response is prognostic and may have clinical implications on the use of additional post-transplant therapy [19].

4. Conclusion

Being the first reported case in our hospital (which is the national cancer center in Khartoum Sudan), proves the rarity of the disease in our country which comes in concordance with the studies done worldwide. Multicenter studies have to be done in order to aggregate a larger sample size to establish the proper treatment and improve the outcome.

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