Case Report

Primary Plasma Cell Leukemia in a 55-Year-Old Nigerian Woman

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Abstract

Plasma cell leukemia (PCL) is a rare and an aggressive disease, accounting for only 2%–3% of all plasma cell dyscrasias. Diagnosis is made by the presence of more than 2×10^9/L plasma cells in the peripheral blood or monoclonal plasmacytosis more than 20% of the plasma cells in the peripheral blood. PCL has limited treatment options comprising of the conventional multiple myeloma (MM) treatment drugs and a very poor prognosis. We report a case of a 55-year-old woman who presented with a history of high-grade fever, generalized weakness, petechial rashes, and transfusion-dependent anemia of about 3 months' duration. Peripheral blood film revealed moderate leukocytosis with 30% plasma cells. Bone marrow aspirate also showed significant plasmacytosis. Immunophenotyping confirmed peripheral blood plasmacytosis. The patient initially responded to chemotherapy but succumbed to the disease.

Keywords: Immunophenotyping, plasma cell dyscrasia, plasmacytosis, primary plasma cell leukemia

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Introduction

Primary plasma cell leukemia (pPCL) is a rare plasma cell dyscrasia (PCD) which is highly aggressive and with a very poor outcome. pPCL arises *de novo*, unlike the secondary type which arises secondary to a preexisting multiple myeloma (MM). About 60%–70% of PCL are primary and the remaining 30%–40% is made up of secondary PCL (sPCL).[1] Since sPCL is a leukemic transformation of MM, that is, it progressed from background MM and not a separate entity on its own, it follows that pPCL is the rarest form of PCD.[1] It is also the most aggressive type of PCD with a high propensity of having extramedullary disease and patients often presenting with organ enlargement and cytopenias.[2] In some cases, patients become transfusion dependent, requiring 2 or more units of packed red cells in a month over 3 months. There are limited data on randomized trials for pPCL definitive treatment, and oftentimes, the conventional multiagent myeloma drugs such as vincristine, adriamycin, and dexamethasone are used still with limited benefit.[2] Several clinicians have tried different combinations of standard MM drugs including a combination of the novel agents with inconsistent reports.[1,2] Nigeria, a country still faced with diagnostic challenge in addition to out-of-pocket payment for health-care services. In the retrospective studies conducted by two independent researchers in Nigeria, the prevalence of PCL was reported to be 0.5%–3.3% of all PCDs; however, there was no distinction to whether it was primary disease or secondary to an existing MM.[3,4] To the best of our knowledge, this is the first case report on pPCL in Nigeria. We present a case of pPCL seen at the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria, in March 2018 because of its rarity and to highlight the diverse and unusual clinical and laboratory features as well as unfavorable outcome despite the use of the novel agent, hence the need for a review of treatment options.

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Case Report

A 55-year-old female, presented through the Accident and Emergency Department of UNTH, has been referred from a peripheral hospital with a 3-month history of symptomatic thrombocytopenia [Figure 1], transfusion-dependent anemia, recurrent fever, and productive cough. Significant findings on examination were moderate-to-severe pallor, generalized petechial and ecchymotic patches; there was no peripheral lymphadenopathy, but the spleen enlarged to 10 cm below the left costal margin. At presentation, she was afebrile (37°C.), pulse rate was 111 beats/min (full volume, regular), respiratory rate was 24 cycles/min, and blood pressure was 80/60 mmHg. There were no complaints of bone pain, and no bone tenderness was elicited.

Investigation results were as follows: hemoglobin level: 6.2 g/dL, white blood cell count: 16.6 × 10^9/L, and platelet count: 46 × 10^9/L; peripheral blood film (PBF) review showed rouleaux formation, mild leukocytosis comprising 30% plasma cells and severe thrombocytopenia; erythrocyte sedimentation rate was normal; and bone marrow aspirate was normocellular but showed plasmacytosis of more than 50% with numerous abnormal forms (numerous immature-looking, Mott and flame cells) present and decreased erythropoiesis, myelopoiesis, and megakaryopoiesis [Figure 2]. Similarly, bone marrow biopsy revealed significant plasmacytosis. There was a prominent distinct band in the gamma-globulin region on serum protein electrophoresis. Liver enzymes were essentially within normal reference limits. There was an increased total protein with reversal of albumin-to-globulin ratio (0.16). Serum urea was raised (23.5 mmol [2.5–8.5]) and creatinine was also high (274 mol/L [44.2–194]). Serum uric acid was elevated (0.62 mmol/L [0.08–0.4]) and serum calcium (corrected) was elevated (3.1 mol/L [2.2–2.8]). The urine was positive for Bence Jones protein. X-ray skeletal survey showed slight lytic lesions in the lumbar vertebrae only, and the skull and other bones showed no obvious bone lesions on X-ray [Figure 3]. Immunoglobulin quantitation showed lgA to below – 20 mg/dl (70–400), lgG was markedly raised – 3402 mg/dL (70–1600), and IgM was absent – 0 mg/dl (40.230). Beta-2 microglobulin level was high (20 mg/dL [1–3 mg/L]). The neoplastic cells were shown to express the following surface markers: CD38+, CD56−,

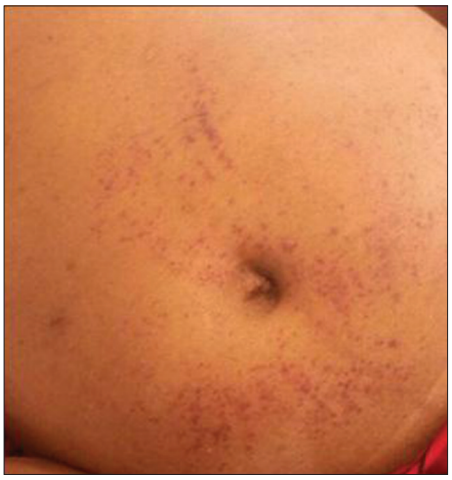

Figure 1: Petechial hemorrhages around the umbilicus

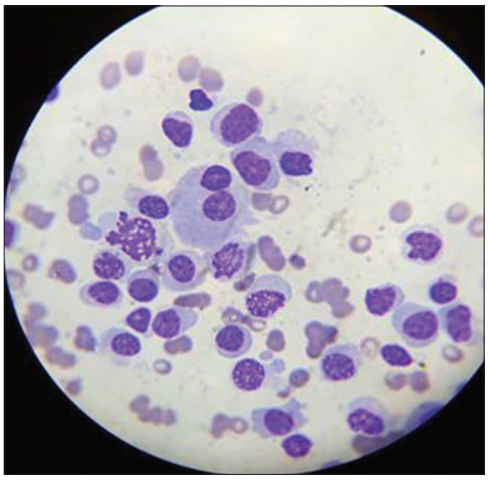

Figure 2: Bone marrow aspirate showing abnormal plasma cells

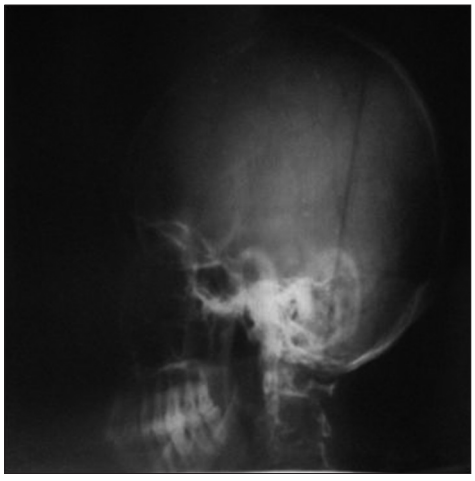

Figure 3: Skull X-ray free of "punched out" lesions

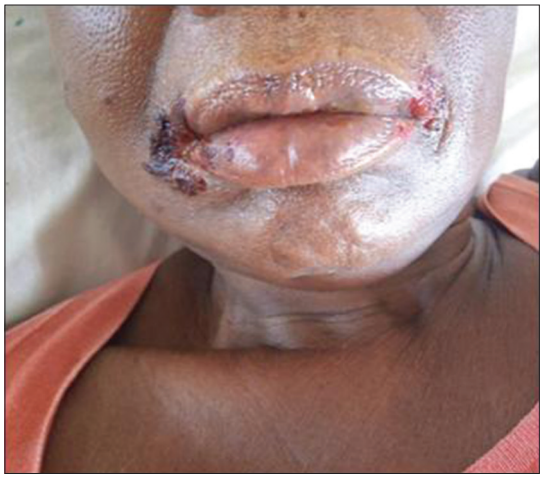

Figure 4: Vesiculopapular lesions on the mouth

CD138−, and CD20+. Sputum microscopy and culture yielded significant growths of *Klebsiella* spp. and *Staphylococcus aureus*. She developed severe low back pain about 12 days into hospital admission. Circumoral vesiculopapular lesions with anal and pubic area involvement also erupted while the patient was on admission [Figure 4].

A diagnosis of pPCL was made to rule out amyloidosis. Management was multidisciplinary. She received supportive care with intravenous fluid rehydration, antibiotics, anticoagulants, and bisphosphonates. She received a total of 12 units of packed red cells (8 prior to presentation and 4 on admission) during the period of her illness. Initially, she required a unit 2 weekly and then worsened to 2–3 units weekly. She also received platelet concentrate while on admission. She was subsequently commenced on bortezomib, thalidomide, and dexamethasone (VTD) regimen. The renal involvement was managed conservatively by the nephrology team. The patient initially responded to treatment, showed remarkable clinical improvement, and became less transfusion dependent, as transfusion requirement dropped from 3 units in the week preceding commencement of the treatment to 1 thereafter but required a unit of platelet concentrate. She deteriorated from about the 12th day of the first cycle of chemotherapy. Our patient finally succumbed to the illness 1 month after commencement of chemotherapy.

Discussion

pPCL is a very rare subtype of PCD, and patients present at a younger age (10 years earlier) than they do in MM or sPCL.[2] Our patient was 55-year-old and was the first case of pPCL diagnosed in our center and indeed the first to be reported in Nigeria to the best of our knowledge. pPCL has an acute onset and rapid disease progression, and patients have a poorer performance status at diagnosis than those with MM.[1,5,6] This was the case with our patient – symptoms occurring suddenly and rapidly. In pPCL, there is often rapidly worsening anemia and thrombocytopenia due to the suppression of normal hemopoiesis in the bone marrow, which is infiltrated by the malignant plasma cells.[1,7,8] Our patient was already symptomatically thrombocytopenic and transfusion dependent at presentation. Bone lesions are absent or mild in pPCL as against MM[9] or sPCL. In the index patient, mild lytic lesions were noted in the lumbar region only.

In pPCL, there is frequently extramedullary involvement which could be due to decreased expression of cell adhesion molecules, such as CD56, aiding the migration of leukemic plasma cells out of the bone marrow microenvironment.[9,10] Our patient presented with splenomegaly which may be resulting from extramedullary involvement, and at the same time, the splenomegaly might have contributed to the cytopenia. Whereas in sPCL, extramedullary diseases are infrequent but they present with worse bone lesions. For our patient, immunophenotyping showed the neoplastic cells to be CD38+, CD56−, CD138−, and CD20+. As seen in the present case, PCL cells are known to show a low expression of the cell adhesion molecule CD56, which suggests a poorer prognosis.[9,11] This was associated with the peripheral plasmacytosis. Likewise, unlike in MM, the plasma cells in PCL are more likely to express CD20, CD45, and CD23 than the typical CD17 and CD117, a picture prevalent among patients with t (11;14).[2,12] Unfortunately, we could not search for all these CD markers as well as cytogenetics for the suspected translocation due to financial constraint since the patient was paying out of pocket. In addition, plasma cells typically express CD138; this expression decreases from monoclonal gammopathy of undetermined significance through MM to PCL as a marker of immaturity.[2] It is not surprising that in this index case, the neoplastic plasma cells had decreased expression of CD138, bearing in mind that majority of the plasma cells on her PBF appeared immature. This notwithstanding, the high expression of CD38 supports that they are probably plasma cells.

Survival is very poor in pPCL; 28% of patients die within 1 month of being diagnosed.[13] The average survival for pPCL is 11.2 months.[14] The goal of treatment is usually to prolong survival. No standard definitive treatment protocol has been developed for pPCL, and the treatment is usually the same as that of MM. Lately, bortezomib-based regimens have replaced intensive multidrug chemotherapy regimens that include alkylating agents but still with little success.[15] Our patient passed on about 1 month into treatment despite having been commenced on VTD regimen.

Conclusion

This is a very uncommon case with a very dramatic presentation. It demonstrates the aggressiveness of pPCL. Persistent anemia and thrombocytopenia with a background suspicion of PCD should raise the index of clinical suspicion and necessitate appropriate investigation to rule out MM and initiate prompt management. The outcome is poor even with commencement of therapy. There is a need for further research to find novel targeted therapies as there are limited benefits from using conventional treatments in pPCL.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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