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Case Report

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Rapidly Progressing Plasma Cell Leukemia with Underlying Plasmablastic Morphology: A Rare Case Report of a 25-Year Old Male

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ABSTRACT

Multiple myeloma constitutes a wide spectrum of diseases ranging from slow-growing monoclonal gammopathy of undetermined significance to rapidly progressing plasma cell leukemia. It is a very rarely diagnosed hematological malignancy in those less than 30 years.

A 25-year-old male presented with complaints of fatigue, low-grade fever. On investigations, he was found to have bicytopeina and features of tumor lysis syndrome. This was initially thought to be consistent with a diagnosis of acute leukemia. Upon further analysis with bone marrow biopsy, serum protein electrophoresis, and immunofixation, the rare diagnosis of IgG myeloma with plasmablastic morphology was confirmed. However, it rapidly progressed and peripheral smear started showing clusters of plasma cells. Despite aggressive treatment, the patient succumbed to the aggressive plasma cell leukemia with an underlying plasmablastic morphology.

This case highlights the possibility of myeloma as one of the differentials in young patients especially the rare plasmablastic variant that can get misdiagnosed as acute leukemia. This aggressive morphology may also show rapid progression to plasma cell leukemia and has an adverse prognosis.

Keywords: Multiple myeloma; Plasmablastic; Plasma cell leukemia

INTRODUCTION

Multiple myeloma accounts for 18% of all hematological malignancies and is considered a malignancy of old age with the median age of presentation being 70 years[1]. It accounts for only 12% of malignancies at an age less than 50 years and 0.3% of malignancies at less than 30 years[2]. Plasma cell dyscrasias constitute a wide spectrum of diseases from monoclonal gammopathy of undetermined significance (MGUS) to multiple myeloma (MM) to plasma cell leukemia.

We present a case of a young patient diagnosed with a rapidly progressing disease that was initially thought to be acute leukemia, which forms the most common blood disorder in this age group. It, however, turned out to be a plasma cell dyscrasia. It was a very aggressive disease that is less likely to be seen in the biology of multiple myeloma.

Case presentation

A 25-year-old male presented with complaints of fatigue and low-grade fever for 2 months. The outside evaluation had revealed bicytopenia (anemia, thrombocytopenia) for which he was

referred to our center. Routine lab investigations revealed Hemoglobin of 8.2 g/dl, total leukocyte count of 10.7 x 10^9/l, platelet count of 16 x 10^9/L, and peripheral smear showed scattered atypical cells (3%). The biochemistry showed serum creatinine of 2.0 mg/dl, uric acid 13.1 mg/dl, corrected calcium level of 12.06 mg/dl, normal potassium and high lactate dehydrogenase (LDH) of 1131 U/L. Testing for Human immunodeficiency virus (HIV) was negative. He had no other medical diseases or a history of cancer in the family. Considering the patient's age with a peripheral smear showing atypical cells, we contemplated a provisional diagnosis of acute leukemia with tumor lysis syndrome (TLS) and likely a T- lymphoblastic leukemia considering the presence of hypercalcemia. TLS was managed with hydration and Rasburicase and additional Calcitonin spray for hypercalcemia correction. Bone marrow aspiration (BMA) showed occasional scattered blasts (5%), residual erythroid and myeloid series increased with a mild increase in plasma cells. A detailed discussion with pathologist concluded that these plasma cells could be reactive and final diagnosis is not feasible given the less blast percentage, hence it was decided to do a repeat bone marrow examination. The second BMA showed 80% plasma cells and bone marrow biopsy showed hypercellular marrow, multiple focal collections of large neoplastic cells with high nuclear/cytoplasmic ratio, vesicular nuclei, prominent nucleoli indicating a diagnosis of high-grade plasma cell myeloma (Plasmablastic type) (Figure 1). Cytogenetic analysis revealed solitary metaphase with add(14)(q32) suggestive of a malignant clone (Figure 2). Further testing with Fluorescence in situ hybridization (FISH) could not be done due to its lack of availability at our center. The skeletal survey showed multiple lytic lesions in the skull and humerus. Serum protein electrophoresis (SPEP) showed an M band of 5.14 g/dl with IgG and lambda bands on immunofixation. He was started on high-dose steroids, bisphosphonates and was planned for chemotherapy with Bortezomib, Thalidomide, Dexamethasone (VTD). However, his symptoms worsened over the subsequent days with worsening renal function, hyperuricemia and hypercalcemia despite treatment. The peripheral smear at this time showed up to 19% plasma cells (Figure 3). He succumbed to this rapidly progressing disease of likely plasma cell leukemia with an underlying plasmablastic morphology.

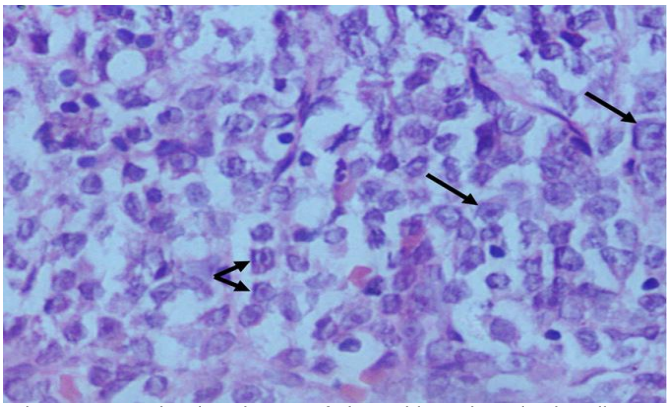

Figure1. BMA showing clusters of plasmablasts (neoplastic cells with high nuclear/cytoplasmic ratio, vesicular nuclei and prominent nucleoli)

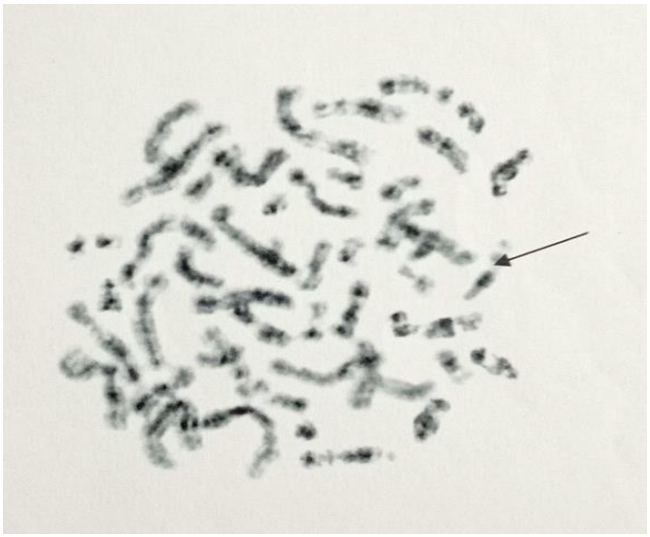

Figure 2. Cytogenetic by G banding showed a solitary metaphase with multiple marker chromosomes and add (14)(q32).

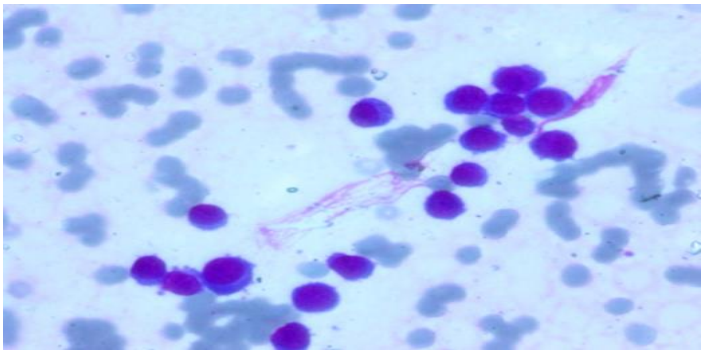

Figure 3. Peripheral smear showing clusters of plasma cells with eccentric nucleus and abundant basophilic cytoplasm. Background shows rouleaux formation.

DISCUSSION

Plasma Cell dyscrasias are diseases of the elderly and unlike other blood cell disorders; they normally follow a very indolent course with more slowly dividing cells. There are few variants like Plasmablastic Myeloma (PM) and Plasma Cell Leukemia (PCL) that have not been formally classified but have been described in the literature.

As per the recent SEER database of 2012-2016, the incidence of MM for ages 20-34 years was 0.5% [3]. One of the initially reported case series from Mayo Clinic showed MM frequency of 0.3% in less than 30 years that is more likely to be Immunoglobulin (Ig) D disease and had better outcomes [2,4]. Usha et al. reported on 14 cases of myeloma in young patients (<40 years) presenting mostly with bone symptoms, anemia, and mostly IgG disease[5]. Among these early reported cases of MM in young patients, Clough et al. reported an aggressive presentation of a 24-year old female with renal failure, pallor, ecchymoses and atypical plasma cells in peripheral smear [6]. Like our patient, they also observed rapid progression of the disease with worsening hypercalcemia and renal failure leading to death within months of diagnosis. A case series by Costello identified high-risk features in young adults with 80% presenting in an advanced stage, 10% with plasma cell leukemia and a relatively worse outcome compared to older patients[7].

MM is usually a slow proliferating tumor with a low risk of tumor lysis syndrome. Few studies have reported spontaneous TLS in myeloma patients and identified hyperproliferative disease, higher immature plasma cell, plasmablasts, increased LDH and poor cytogenetics as risk factors [8,9].

Only conventional cytogenetics was done for our patient that showed add(14)(q32). Further FISH testing would have been required to identify the exact translocation. Sawyer et al found that patients who had add(14)(q32) chromosomes by G-banding karyotype when refined by Spectral karyotyping (SKY) and FISH showed recurring known translocations [10].

Plasmablastic myeloma

Unlike lymphomas that have a recognized classification based on morphological features, multiple myeloma morphological differences are not well recognized as a feature to prognosticate or plan treatment. However, morphological differences have been reported in myeloma and correlated with outcomes in various studies. Bartl et al were among the first to put forward a histological classification based on 674 patients of MM. They initially defined a low-grade plasmacytic and high-grade plasmablastic group based on plasma cell maturity and infiltration of marrow by plasma cells[11]. They further considered the size, cytoplasmic and nuclear characteristics to divide myeloma into six groups - Marschalko, small cell, cleaved, polymorphous, asynchronous, and blastic type. Among these, plasmablastic constitutes the high-grade disease with a median survival of nine months from onset of symptoms [12].

Based on Wright stained bone marrow aspirated slides, MM cells were classified by Greipp et al into mature, intermediate, immature, or plasmablastic type[13]. It was called as plasmablastic types if there were 2% or more plasmablastic myeloma cells. These plasmablasts had a large nucleus, fine reticular chromatin, large nucleolus and less cytoplasm with little or no hof region. They also noticed worse survival with this histology when compared to the other types (median overall survival 10 vs 35 months, $P < 0.05$). They further confirmed the aggressive biology and adverse prognostic implication of this subtype by reviewing the bone marrow of patients in the Eastern Cooperative Oncology Group (ECOG) trial E9486. Plasmablastic type constituted 8.2% with a higher incidence of anemia, hypercalcemia, renal insufficiency, higher beta 2 microglobulin, and serum interleukin 6 receptor levels and ras mutations. They also studied the tumor kinetics using plasma cell labeling index (PCLI) that measures the percentage of plasma cells in the S phase and found it to be higher in plasmablastic type [14]. Srija et al. had reported a young patient of plasmablastic myeloma with rapidly progressive renal failure that unlike our patient had a good response to bortezomib and dexamethasone[15].

Plasma cell leukemia

It is a very rare form of plasma cell dyscrasia accounting for <5% of primary diagnosis. A review of around 900 MM patients by Kyle et al showed a

median age of PCL to be ten years less than MM. There are very few reported cases of PCL among young adults[16]. It can either present as de novo primary PCL or as secondary PCL after transformation from MM. Majumdar et al. studied 28 cases of PCL, majority were primary disease. However, they reported that 30% of these were misdiagnosed as either acute leukemia or as leukemic phase of lymphoma. The time interval from symptom onset to diagnosis was 3 weeks to 11 months [17]. Our patient had an aggressive disease that rapidly progressed with plasma cells in the peripheral blood within a month of presentation.

PCL show many cytogenetic abnormalities with increased frequency of t(11;14), t(14;16) and13q deletions[18]. Though it is more commonly reported with light chain, Immunoglobulin IgE and D, our patient had IgG type. These patients have a more aggressive disease with high tumor load, higher LDH, hypercalcemia and high risk of presenting with TLS. The bone marrow is extensively infiltrated by plasma cells more of high-grade anaplastic and plasmablastic morphology, hence suppressing other lineages and presenting more commonly with anemia, thrombocytopenia[19] like our patient. Prognosis of PCL is very poor with a median survival of 2–8 months.

Gluzinski and Reichentein reported the first case of PCL in 1906[20] and Kyle first defined the criteria for its diagnosis[21]. Kyle's criteria require 20% circulating plasma cells in the peripheral blood and/or an absolute plasma cell count of 2.0 x109/L, with evidence of monoclonal gammopathy. A recent publication suggests that if the diagnostic criteria were reduced to 5% plasma cells and/or an absolute count of >0.5x109/L, more patients could be diagnosed earlier as this entity needs aggressive combination chemotherapy at the earliest.

In conclusion, we must consider the possibility of myeloma even in young patients as they may present with the more aggressive histology that requires early identification and aggressive treatment. The morphologic evaluation is useful in identifying cases that will manifest aggressive clinical behavior. It was a difficult diagnosis as it is a rare disorder at this age. Our patient's blood parameters showed bicytopenia and based on his age, we thought a provisional diagnosis of acute leukemia. However, bone marrow evaluation revealed plasmablastic myeloma. Also, the disease had a very rapid progression that is unlikely seen in Plasma Cell disorders.

Whether plasmablastic morphology retains its prognostic significance in patients treated with newer agents like immunomodulators and proteasome inhibitors is unknown and needs further studies. However, it may still be important to identify these morphological indicators to better understand the tumor biology, natural course of disease and its likely response to treatment.

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