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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 of age.

A 25-year-old male presented with complaints of fatigue and low-grade fever. On investigation, he was found to have bicytopeina and features of tumor lysis syndrome. Initially, this was thought to be indicative of acute leukemia. However, upon further analysis with bone marrow biopsy, serum protein electrophoresis, and immunofixation, it was determined that the patient had an IgG myeloma with plasmablastic morphology. It rapidly progressed and the peripheral smear started showing clusters of plasma cells suggesting a picture of plasma cell leukemia. The patient succumbed to this aggressive disease despite treatment.

This case illustrates that myeloma should also be included in the differential diagnosis for young patients, especially the rare plasmablastic variant, which can be misdiagnosed as acute leukemia. The aggressive morphology also tends to show rapid progression to plasma cell leukemia, which has a poor 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 less than 50 years of age and 0.3% of malignancies at less than 30 years of age[2]. Plasma cell dyscrasias constitute a wide spectrum of diseases from monoclonal gammopathy of undetermined significance (MGUS) to multiple myeloma (MM) and 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 is the most common blood disorder in this age group. However, it turned out to be a plasma cell dyscrasia with a very aggressive nature, which is less likely to be seen in multiple myeloma biology.

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

a peripheral smear showed scattered atypical cells (3%). The biochemistry showed serum creatinine of 2.0 mg/dl, uric acid of 13.1 mg/dl, corrected calcium level of 12.06 mg/dl, normal potassium, and a high lactate dehydrogenase (LDH) of 1131 U/L. Testing for the 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) and biopsy showed occasional scattered blasts (5%), erythroid, myeloid series and mildly increased plasma cells. A detailed discussion with the pathologist concluded that these plasma cells could be reactive. Due to the low blast percentage, no final diagnosis was made until a repeat bone marrow examination was performed. The second BMA showed 80% plasma cells and bone marrow biopsy revealed a hypercellular marrow. There were multiple focal collections of large neoplastic cells with high nuclear/cytoplasmic ratio, vesicular nuclei and prominent nucleoli, which led to the diagnosis of high-grade plasma cell myeloma (plasmablastic type) (Figure 1). Cytogenetic analysis revealed a 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, and bisphosphonates and was planned for chemotherapy with Bortezomib, Thalidomide, and Dexamethasone (VTD). In spite of treatment, his condition deteriorated over the subsequent days with worsening of renal function, hyperuricemia, and hypercalcemia. The peripheral smear at this time showed an increased number of plasma cells (up to 19%) suggesting a picture of plasma cell leukemia (Figure 3). He succumbed to the rapidly progressing disease characterized by its aggressive plasmablastic morphology.

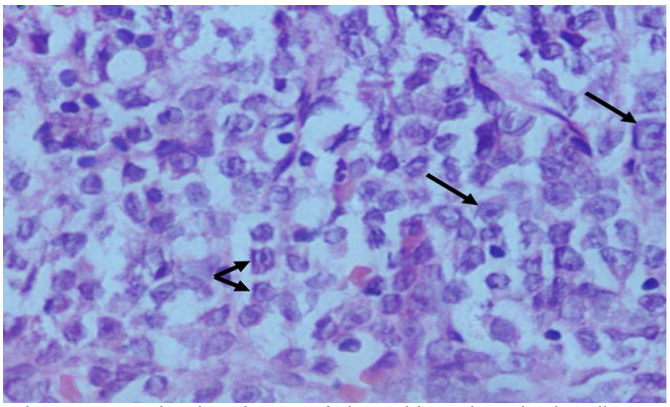

Figure1. BMA showing clusters of plasmablasts (neoplastic cells with high nuclear/cytoplasmic ratio, vesicular nuclei and prominent nucleoli)

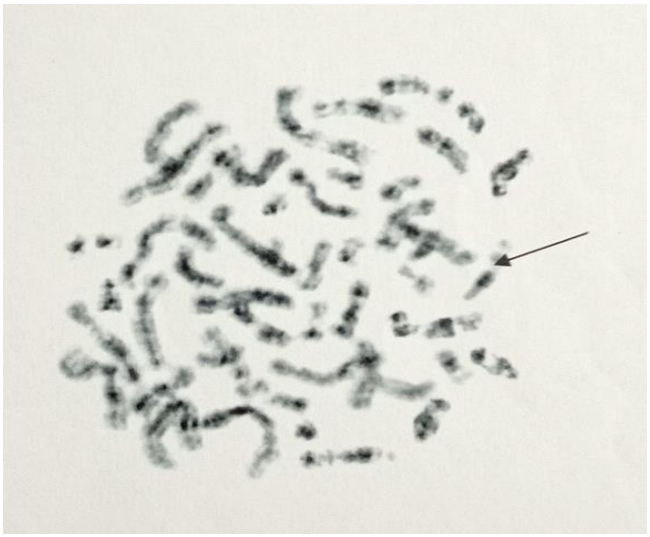

Figure 2. Cytogenetics by G banding showed solitary metaphase with multiple marker chromosomes and add (14)(q32).

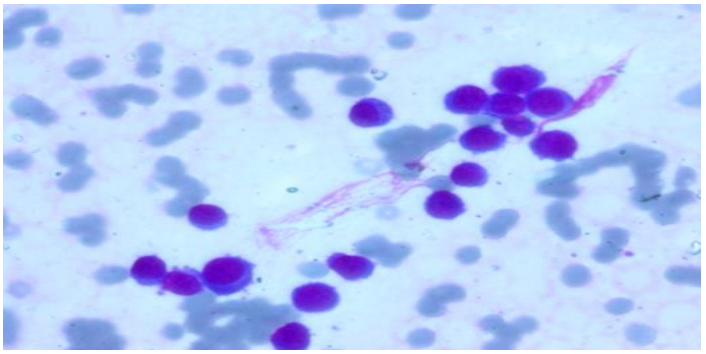

Figure 3. Peripheral smear showing clusters of plasma cells with an eccentric nucleus and abundant basophilic cytoplasm. The background shows rouleaux formation.

DISCUSSION

Plasma cell dyscrasias are diseases of the elderly and unlike acute leukemia; they follow a very indolent course with slowly dividing cells. There are a few variants like Plasmablastic Myeloma (PM) and Plasma Cell Leukemia (PCL) that have not been formally classified but are described in 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 a MM frequency of 0.3% in less than 30 years was more likely to be Immunoglobulin (Ig)D disease and had better outcomes. [2,4] In a study by Usha and colleagues, they reported 14 cases of myeloma in young patients (<40 years) presenting mainly with bone symptoms, anemia, and predominantly IgG disease[5]. Among the 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. A few studies have reported spontaneous TLS in myeloma patients and identified hyperproliferative disease, higher immature plasma cells, plasmablasts, increased LDH and poor cytogenetics as risk factors [8,9].

The conventional cytogenetics detected add(14)(q32) chromosome in our patient. Further FISH testing would have been required to identify the exact translocation. Sawyer et al. found that patients identified by G-banding karyotype with add (14)(q32) chromosome showed recurring known translocations when refined by Spectral karyotyping (SKY) and FISH[10].

Plasmablastic myeloma

Unlike lymphomas having a recognized classification based on morphological characteristics, 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 researchers to put forward a histological classification based on 674 patients with MM. They initially defined a low-grade plasmacytic and a 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 the 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 plasmablastic type if there were 2% or more plasmablastic myeloma cells. These plasmablasts had a large nucleus, fine reticular chromatin, and less cytoplasm with little or no hof region. They also noted a worse survival with this histology compared to other types (median overall survival 10 Vs. 35 months, $P < 0.05$). They further confirmed 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. The plasmablastic type constituted 8.2% of the study population, with a higher frequency of anemia, hypercalcemia, renal insufficiency, higher beta 2 microglobulin, serum interleukin 6 receptor levels and ras mutations. They also studied the tumor kinetics using the plasma cell labelling index (PCLI) that measures the percentage of plasma cells in the S phase and found it to be higher in the plasmablastic type[14]. Srija et al. reported a young patient diagnosed with plasmablastic myeloma with rapidly progressive renal failure who, unlike our patient, had a positive 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 be present as a de novo primary PCL or as a secondary PCL after transformation from MM. Majumdar et al. studied 28 cases of PCL, the majority of whom showed primary disease. However, they reported that 30% of patients were misdiagnosed as having either acute leukemia or the 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 has a high prevalence of cytogenetic abnormalities, including 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 more aggressive disease with a high tumor load, higher LDH, hypercalcemia, and a high risk of presenting with TLS. The bone marrow is extensively infiltrated by plasma cells of high-grade anaplastic and plasmablastic morphology, hence suppressing other lineages and presenting more commonly with anemia, thrombocytopenia[19] like our patient. The 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 of a provisional diagnosis of acute leukemia. However, bone marrow evaluation revealed plasmablastic myeloma. Also, the disease had a very rapid progression that is unlikely to be 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, the natural course of disease and its likely response to treatment.

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