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Case Report

A Rare Case of Non Secretory Plasma Cell Leukemia with Unusual Morphology and Aberrant Expression of CD23 and CD56

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Abstract

Primary non-secretory Plasma cell leukemiaisa rare diagnosis with only few cases reported so far. Here we report a case of a non secretory Plasma cell leukemia diagnosed on flow cytometry, as atypical morphology and negative serum and urine protein electrophoresis made it difficult to come to a conclusive diagnosis based on morphology.

INTRODUCTION

Plasma cell leukemia (PCL) is a rare and aggressive variant of Multiple Myeloma (MM) with poor prognosis. Its incidence is believed to be less than 1 case/million [1]. Rarely, there is absence of detectable M component in the serumor urine, such cases known as non secretory Plasma cell leukemia. Non secretory MM account for only 1% of total MM with very few cases reported till date [2].

Non secretary plasma cells may be especially difficult to diagnose if they show abnormal morphology. Immuno-phenotyping and immunohistochemistry have played a great role in modern diagnostics to accurately identify the leukemic cells [3]. Here, we report a case of primary non-secretory plasma cell leukemia with atypical morphology.

CASE PRESENTATION

A 56-year-old lady presented with shortness of breath, generalised weakness and facial puffiness since 2 months. There was no history of fever, infection, diabetes and hypertension. On physical examination she had pallor but no icterus. There was no hepatosplenomegaly or lymphadenopathy. Local examination revealed bony tenderness in the back. Subsequently, radiograph of dorso-lumbar spine showed anterior wedging with compression collapse of D11 vertebral body suggesting wedge fracture (Figure 1).

Abdominal Ultrasound did not show any abnormality with normal liver size and echotexture along with anteverted uterus and unremarkable bilateral adnexa. Liver function tests (Serum Bilirubin, SGOT, SGPT, Alk phosphatase) were normal and viral markers were negative. However the renal functions were derranged (B.Urea: 77 mg/dl and S.Creatinine: 5.4 mg/dl)

Subsequently, a hemogram sample along with bone marrow aspirate and biopsy was received. Hemogram sample revealed anemia with leucocytosis and mild thrombocytopenia (Hb: 7.7 g/dl, TLC: 53,000/µl and Platelets: 98,000/µl). Peripheral smear examination showed atypical lymphoid cells constituting 52% of total leucocytes. These cells had high N/C ratio, fine opened up chromatin, inconspicuous nucleoli and scant blue agranularcytoplasm. Some of these cells showed cytoplasmic projections. They were negative for myeloperoxidase and PAS. In addition, polymorphs showed left shift uptilmyelocyte stage (Figure 2) and there were 6 nucleated RBC's per 100 WBC's. The marrow aspirate was also hypercellular and showed infiltration by similar cells as seen in peripheral smear. Cytoplasmic projections were also observed in some of these cells in the marrow as seen in peripheral blood. Based on the above findings, adiagnosis of lymphoproliferative disorder with spill over into peripheral blood was considered, with a possibility HCLv or Splenic Marginal Zone Lymphoma kept in mind (Figure 3-6).

Therefore a FCM analysis was performed with a primary lymphoma panel applied on peripheral blood. The abnormal cluster of cells, constituting around 70%, was negative for CD45 and had a low side scatter. These cells were also negative for CD10, CD19, CD20, FMC7, Surface Kappa and lambda. CD5, CD8, CD4, CD3 and CD7 were also found to be negative thus ruling out primary B and T cell lymphomas. Cytoplasmic MPO, Cytoplasmic CD3 and cytoplasmic CD79a were also negative. However these

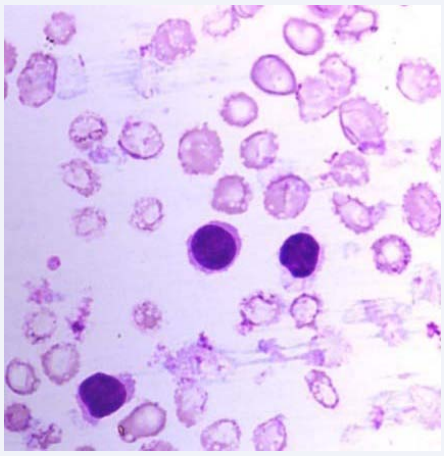

Figure 1 Peripheral smear showing atypical lymphoid cells with cytoplasmic projections; Geimsa 1000X.

cells were positive CD38 and moderately expressed CD23 and CD56. Following this, another tube was put which included CD38 and CD138 along with CD45. Surprisingly, these cells were also positive for CD138 revealing plasma cell nature of these cells. Based on flow cytometry a diagnosis of plasma cell leukemia with atypical morphology and aberrant expression of CD56 and CD23 was made.

Further investigations were done by performing a skeletal survey which revealed multiple lytic lesions on lateral and AP radiograph of skull. However, serum protein electrophoresis (SPE), urine protein electrophoresis (UPE) and immunofixation electrophoresis (IFE) showed no monoclonal proteins Therefore a final diagnosis of Primary non secretory plasma cell leukemia with aberrant expression of CD23 and CD56 was made.

DISCUSSION

Atypical plasma cells sometimes make the diagnosis of PCL difficult and may require an immunohistochemistry or immuno phenotyping to establish a definitive diagnosis [3]. The diagnosis may be made difficult further by the non-secretory (absence of M component) nature of the PCL [4]. Absence of a monoclonal protein in the serum and urine of patients with non-secretory PCL may be a result of (i) an inability to excrete immunoglobin (non-secretors) (ii) low synthetic capacity for immunoglobin (non-producers) (iii) increased intracellular degradation, or (iv) rapid extracellular degradation of abnormal immunoglobins [5]. The molecular basis of non-seceretory myeloma could be due to loss of light chain production (in non-producers) or mutations that cause absence of cysteines required for disulfide bonds [6]. This results in abnormal misfolded light chains, which get retained in the plasma cells due to misfolding and are lysed.

Our case also depicted aberrant expression of CD23 by flow cytometry. Walters et al examined 50 diagnostic PCM bone marrows (including three cases of primary PCL) for CD23 expression by immunohistochemistry [7]. All five CD23 positive cases displayed abnormalities of chromosome 11 by conventional cytogenetics and/or FISH. Four of these cases contained a t (11; 14) (q13; q32), while the fifth case showed a trisomy 11 by conventional cytogenetics. Although CD23 was strongly associated with the t (11; 14) (q13; q32), only 40% of cases with this translocation were $CD23^{+}$. They found no significant association between presenting features within this cytogenetic cohort based on CD23 expression. Cytogenetics could not be done in the present case due to economic constraints.

Examination of a larger set of cases is necessary to assess the clinical relevance of CD23 expression in PCM carrying the t (11; 14) (q13; q32). Although the role of CD23 in PCM is unknown, its expression in a minority of cases could represent a therapeutic target in the subset of positive cases [8].

The present case was CD 56 positive. Several researchers have noted that primary PCL shows less frequent positivity for CD56 as compared to PCM [9]. Kraj et al., found more frequent expression of CD56 in secondary PCL as compared to primary PCL [10]. Tembhare et al., in a retrospective study of Indian population have reported 44% positivity of CD 56 in PCL patients [11].

In the present case, most of the lymphoid cells in peripheral blood had an atypical morphology which made it difficult for diagnosis. Some morphological characteristics seem to be related to a worse prognosis than the usual well-differentiated myeloma [12]. Also in our case, the cells were non-secretory in nature, which is again very rare, as very few cases of primary non-secretory PCL have been reported [4]. In spite of considerable overlap of immunophenotypic markers between multiple myeloma and plasma cell leukemia, significant differences in antigen expression

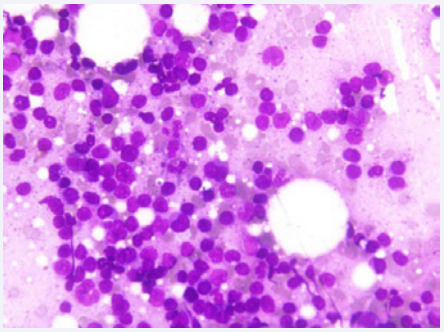

Figure 2 Bone marrow aspirate showing similar cells in marrow; Geimsa 400X.

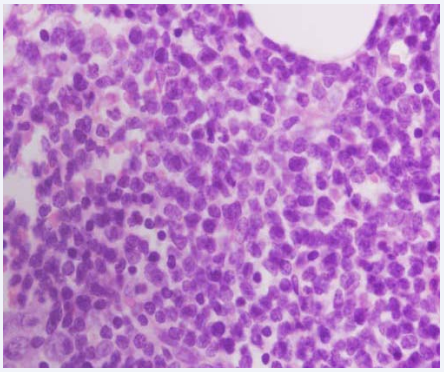

Figure 3 Bone marrow biopsy showing interstitial spread with vesicular nuclei and inconspicuous nucleoli; H & E 400Xarrow.

have been identified which help to differentiate the two variants. Plasma cells in PCL frequently display a more immature phenotype. Immunophenotypically, plasma cells in PCL show the following pattern: CD38+, CD138+, CD79a+, cytoplasmic Ig+, CD20-/+, CD19-, CD45-, CD56-, surface Ig- [13]. However in our case plasma cells were CD56+, CD23+ and CD79a-, cytoplasmic Ig-. Expression of pan-B cell antigen CD20 has been shown in 50% of PCL cases which was negative in our case. Neoplastic cells in marrow and peripheral blood in PCL typically do not express CD56, which is considered to have an important role in anchoring plasma cells to bone marrow stroma. Our final diagnosis was made on flow cytometric immunophenotyping that showed the cells to be bright surface CD38 and CD138 positive and negative for CD45, CD19, CD20, CD10 and surface κ/λ. Accurate diagnosis of primary PCL is essential, as it is an aggressive disease with a short median survival of 2–6 months, with poor response to chemotherapy [14].

SUMMARY

Primary PCL is a rare and aggressive variant of multiple

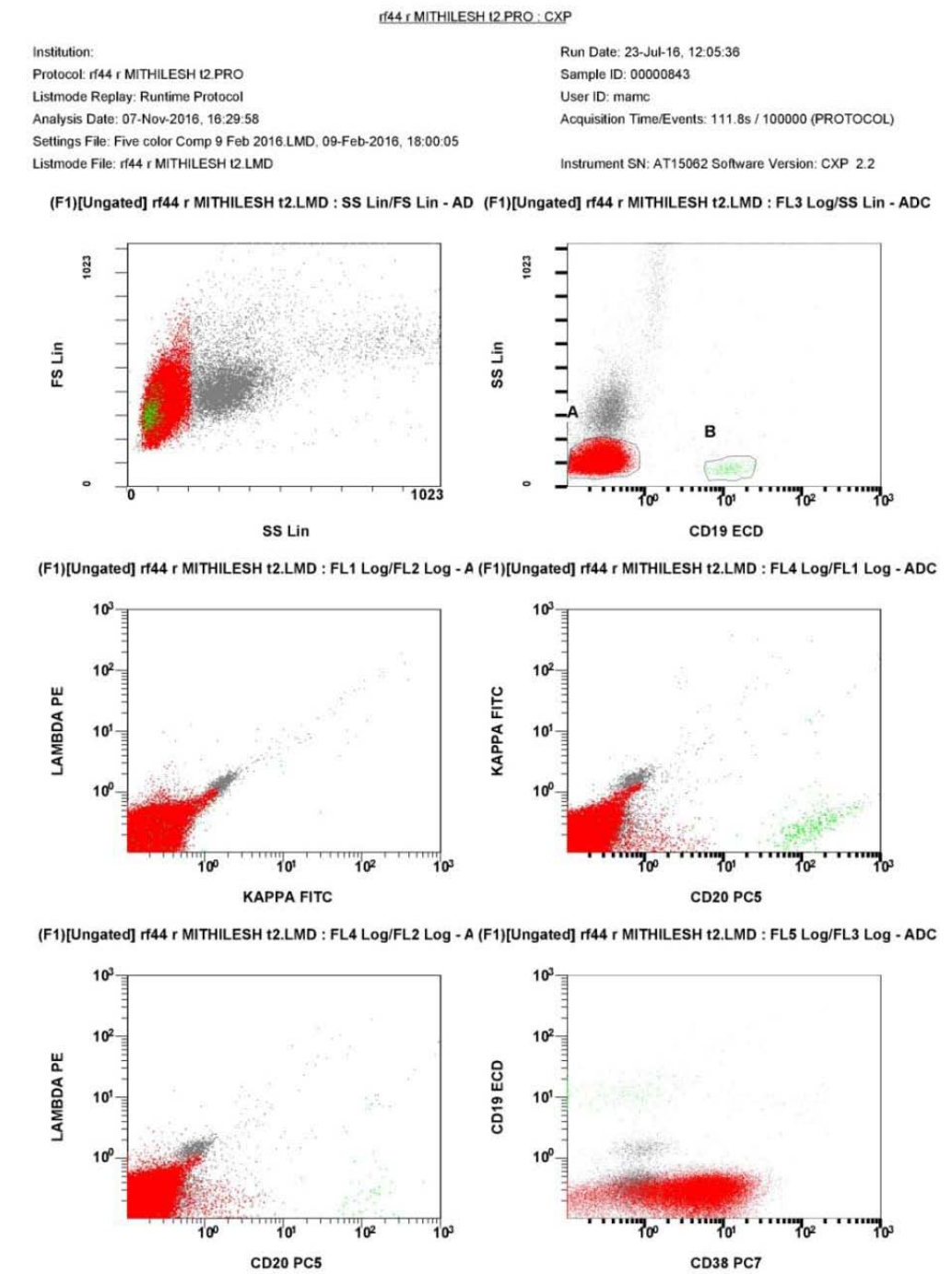

Figure 4 FCM plot showing atypical cells negative for CD19, CD20, s Kappa, s Lambda and positive for CD38.

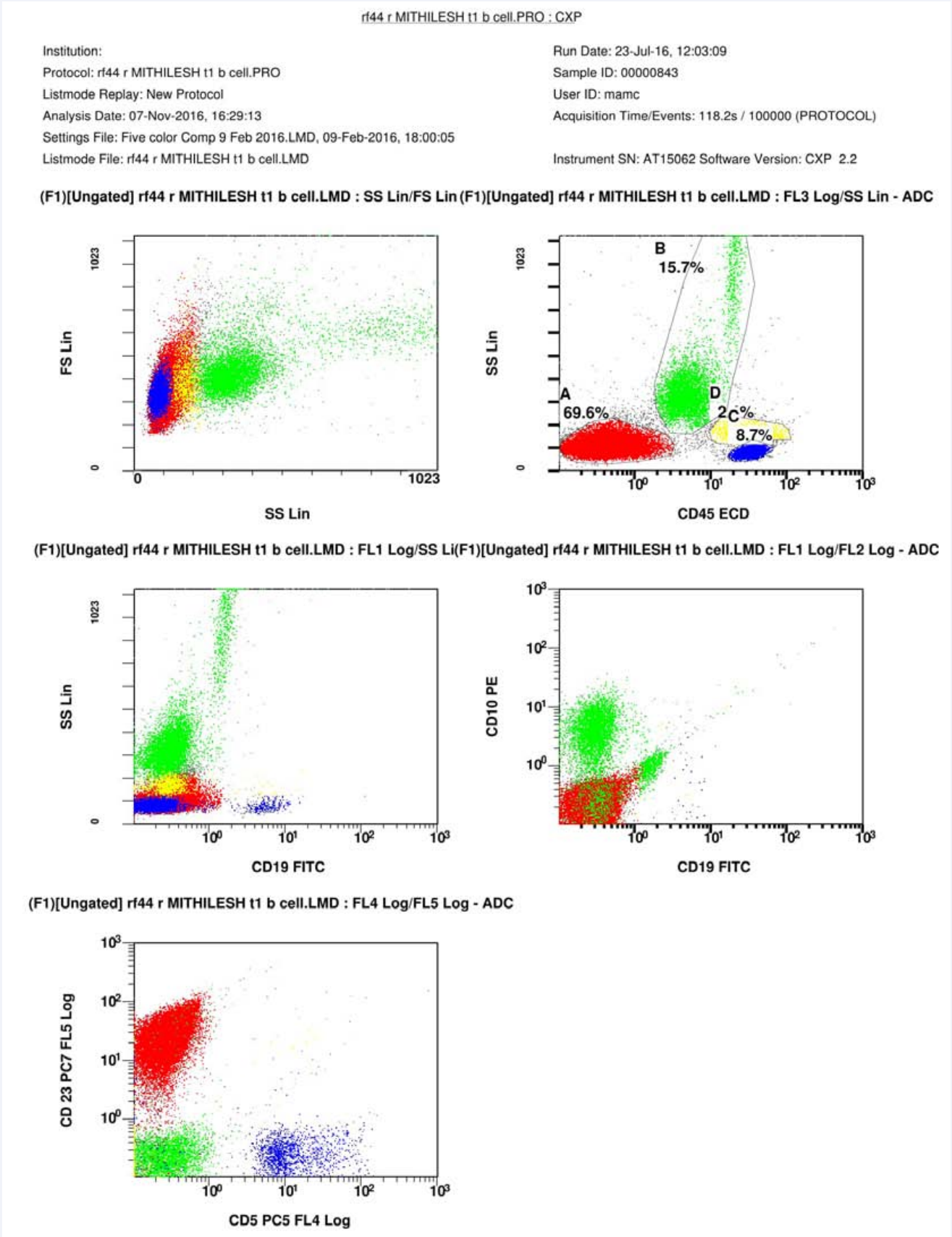

Figure 5 FCM plot showing atypical cells negative for CD10 negative and CD23 positive.

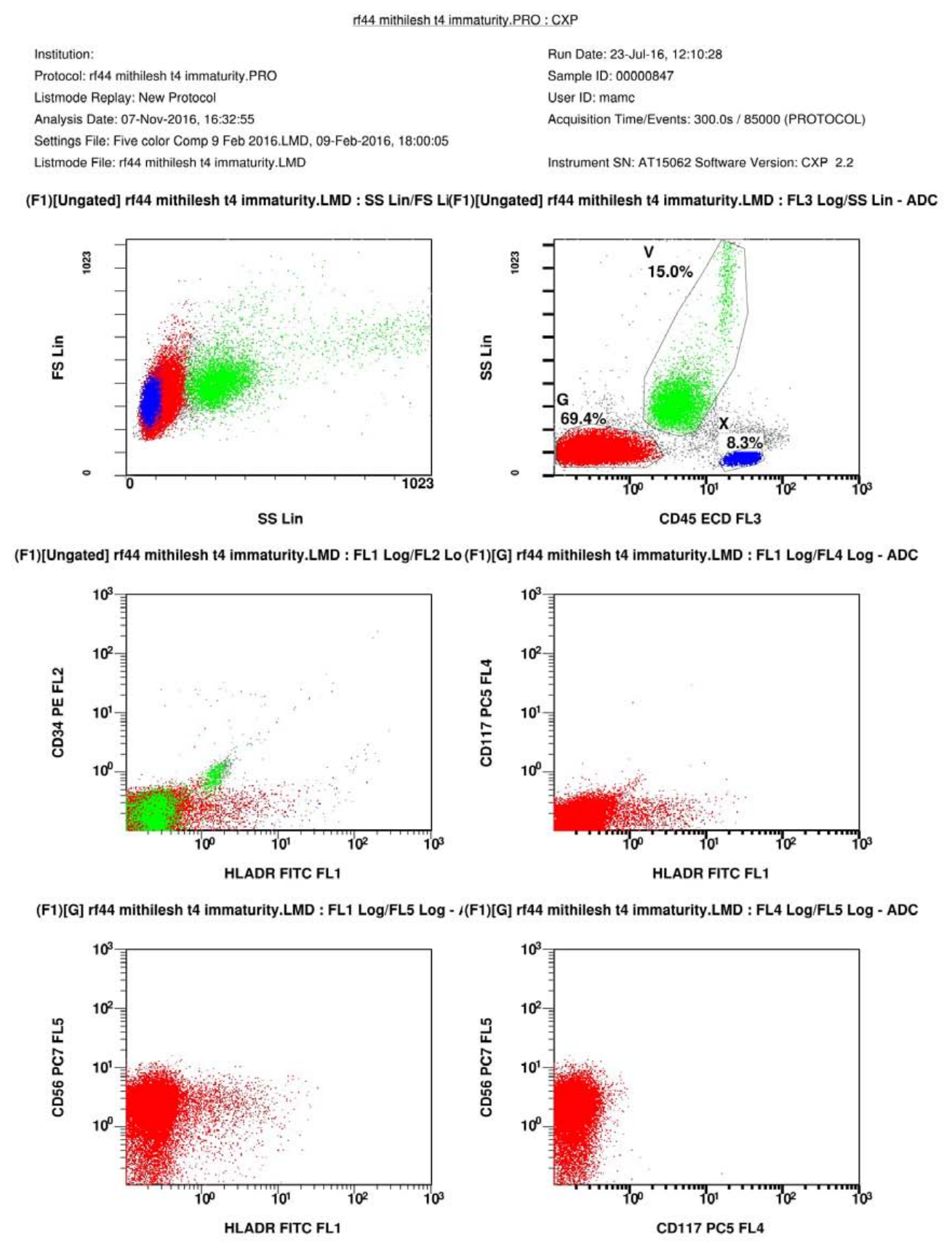

Figure 6 FCM plot showing atypical cells negative for CD117, HLA-DR, and CD34 and positive for CD56.

myeloma with a dismal prognosis. The diagnosis difficulty may be further compounded in cases presenting with atypical morphology and absence of secretion of monoclonal proteins. Flow cytometry is an extremely useful adjunct in such cases and a plasma cell tube should be included in the diagnostic panel if the B and T markers are negative. The case emphasises the need to keep this diagnosis in mind in case of atypical lymphoid proliferations and the importance of flow cytometry in arriving at the correct diagnosis.

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