

Case Report

Two Atypical Cases of Classical Hairy Cell Leukaemia and Hairy Cell Leukaemia Variant: A Case Study

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Abstract

Introduction: Classical Hairy Cell Leukaemia (cHCL) and Hairy Cell Leukaemia variant (HCL-v) are both rare and slow-growing mature B cell neoplasms. According to flowcytometry data, they fall into the group classified as CD5- CD10- B cell lymphoproliferative disorders. **Methods:** Two cases with features atypical to two neoplasms at the time of diagnosis were studied. **Results:** Case 1 was a 15 year old male with right cervical lymph nodes (1x1 cm) in the posterior triangle, a few ecchymotic patches on the arm and a massive splenomegaly. C-reactive protein (CRP) level was 53 mg/dL. Erythrocyte Sedimentation Rate (ESR) was 98 mm/1st hour. Full Blood Count (FBC) revealed typical features of pancytopenia with monocytopenia. The liver and renal profiles were normal. Morphology of bone marrow was suggestive of cHCL. Flowcytometry and BRAF V600E mutation was positive confirming the diagnosis of cHCL. Case 2 was a 55 year old male presenting with moderate splenomegaly and absolute lymphocytosis. The FBC revealed leukocytosis which is commonly seen with monocytopenia. Blood pictures revealed many hairy cells with moderately basophilic cytoplasm and visible nucleoli suggesting HCL-v. Flowcytometry findings and negative BRAF V600E mutation confirmed HCL-v. **Conclusions:** Clinical findings, blood images, morphology of bone marrow, flowcytometric findings and positive BRAF V600E mutation confirmed the diagnosis of cHCL in Case 1 (15 year old boy) making it as a very rare case. The morphological findings on blood, the presence of characteristic CD markers on flowcytometry and negativity of BRAF V600E confirmed the Case 2 as HCL-v, despite having CD10 positivity and monocytopenia.

Keywords: Flowcytometric immunophenotyping, Hairy cell leukaemia, Hairy cell leukaemia variant

Introduction

Hairy cell leukemias (HCLs) are rare, slow-growing mature B cell neoplasms included in the group of CD (cluster of differentiation) 5-CD10- B cell lymphoproliferative disorders representing 2% of lymphoid leukaemias with a characteristic morphologic and immunophenotypic profile [1]. It affects males than females. Classical Hairy Cell Leukaemia (cHCL) has been diagnosed rarely in patients in their 20s, but it is exceptionally uncommon in children [2]. The median age at which cHCL was detected is 52 years.

The cHCL has unique clinical symptoms which help to differentiate it from other B Cell Chronic Lymphoproliferative Disorders (BCLPD). The most common symptoms include; splenomegaly, hepatomegaly, pancytopenia with a few

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circulating neoplastic cells and monocytopenia. Rarely, Hairy Cell Leukaemia (HCL) is asymptomatic at the time of diagnosis [3]. Immunophenotyping plays a major role in diagnosis of cHCL, as hairy cells are characteristically positive for; CD19, CD20, CD79b, CD103 and CD25, bright positive for CD123, CD11c, CD200 and usually negative for CD10, CD5, and CD23. Co-expression of CD11c, CD103 and CD25 is considered as unique for cHCL [3,4].

The BRAF is an oncogene that makes a protein. It helps to control cell growth. The presence of BRAF mutation gene leads to uncontrolled cell growth and cancer. V600E mutation of the BRAF gene can be described as a molecular marker of HCL [5,6]. Absence of CD25, CD123 and CD200 with positive expression of pan B cell antigens, CD11c, bright sIg and CD103 are characteristic immunophenotypic features of the Hairy cell variant (HCL-v) and presence of BRAF V600E mutations have not been documented in HCL-v [1].

The aim of this case study was to describe the atypical patterns of cHCL and HCL-v in very rare type of B cell neoplasms.

Methods

Two cases were studied after obtaining the consent from both patients. Relevant laboratory tests of these two patients were performed after admitting them to the Sri Jayewardenepura General Hospital, Sri Lanka. Bone marrow and peripheral blood specimens of the Case 1 patient were obtained by conventional aspiration or venipuncture procedures and peripheral blood specimens of the Case 2 patient were obtained by venipuncture procedures. Full Blood Count (FBC) was done by Mindray BS 6800 machine in the Department of Haematology. Detection of Serum Lactate Dehydrogenase (LDH) level, liver function tests and renal function tests were

performed by Architech plus C8000 Abbott machine in the Department of Biochemistry. Flowcytometry tests and imaging tests were also performed in the Sri Jayewardenepura General Hospital, Sri Lanka. BD FACS Canto TM II was the flowcytometer and it was configured with three lasers to detect up to eight colours. The computer work-station was equipped with the calibrated machine with quality control. BD FACS Diva software was used to analyze the results.

Results

Case report 1

A 15 year old male patient was admitted to a casualty medical ward in the Sri Jayewardenepura General Hospital, Sri Lanka with the history of fever for four days. He was previously healthy. He did not have abdominal discomfort, loss of appetite or loss of weight, which are the common findings in patients with cHCL. Physical examination revealed right cervical lymph nodes (1x1 cm) in the posterior triangle, few ecchymotic patches on the arm and a massive splenomegaly (15cm below the costal margin) which is a characteristic finding for cHCL. C-reactive Protein (CRP) level was 53 mg/dL. Tests done for viral studies were negative.

His FBC report revealed pancytopenia with anaemia having a hemoglobin level of 8.3 g/dL, thrombocytopenia ($67 \times 10^3/\mu\text{l}$), and leukopenia ($3.68 \times 10^3/\mu\text{l}$). The differential count revealed a predominant lymphocyte count of $2.61 \times 10^3/\mu\text{l}$ (71.1%) and a monocytopenia ($0.08 \times 10^3/\mu\text{l}$ (1.9%). Erythrocyte Sedimentation Rate (ESR) was 98 mm/1st hour. Both liver and renal functions were normal. Serum LDH was normal.

Many atypical lymphoid cells characterized by medium to large cells with villous projections were detected in the blood picture (Figure 1a). His bone marrow aspiration biopsy showed an

abnormal population of lymphoid cells and characterized by high nuclear to cytoplasmic ratio with mature chromatin pattern and variable blue cytoplasm with many villous projections accounting for approximately 60% of the nucleated marrow cells (Figure 1b). The findings of bone marrow trephine biopsy (Figures 1c and 1d) were typical for HCL.

Protein electrophoresis showed a polyclonal increase in the gamma region, suggesting of an inflammatory, infectious or a reactive process. Computed Tomography (CT) scan of the abdomen revealed a massively enlarged spleen (25x10 cm), hepatomegaly (20 cm in

mid-clavicular line), enlarged and homogenous celiac and superior mesenteric lymph nodes. Ultrasound scan of neck identified the presence of multiple bilateral level III and IV cervical lymph nodes.

To confirm HCL, flowcytometry was performed using a bone marrow sample. Live cells were gated by CD45 (Figure 2) and two distinct populations as lymphocytes and granulocytes were identified. Lymphocytes were gated by CD3 and CD19 (Figure 3). B cell percentage was 88.6%, T cells and Natural Killer (NK) cells were 0.8% and 11.5%. Plasma cell percentage was 1.5%.

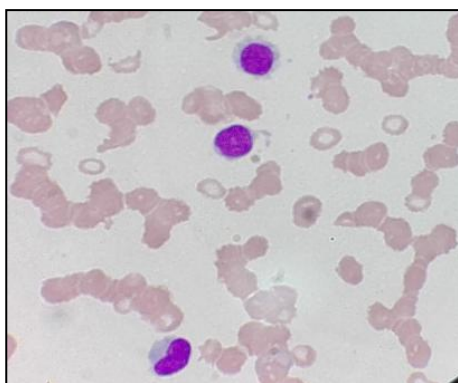


Figure 1a: Morphology of cells in peripheral blood

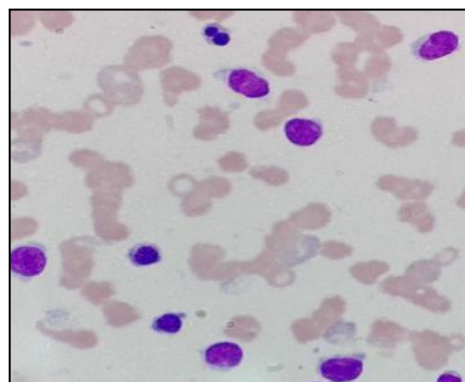


Figure 1b: Morphology of cells in bone marrow

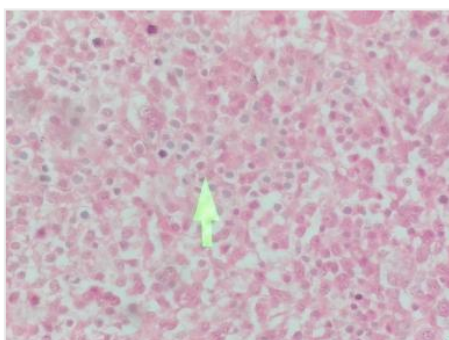


Figure 1c: Morphology of trephine biopsy (H & E Stain)

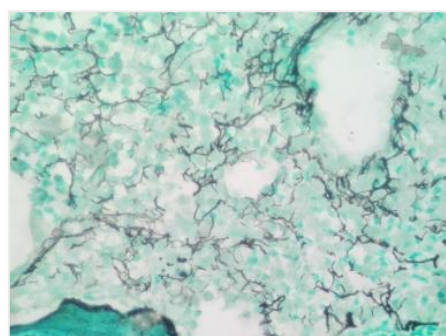


Figure 1d: Morphology of trephine biopsy (Reticulin Stain)

Figure 1: Cell morphology of blood picture, bone marrow aspiration and trephine biopsy in Case 1

The immunophenotypic results of BCLPD and BCLPD HAIRY panels showed positivity for; CD19, smIg Kappa, CD25, FMC7, CD103, and CD123. It also showed bright positivity for CD20,

CD11c and CD200. Both panels are typical for cHCL (Figure 4). Cytogenetics confirmed the positive BRAF V600E mutation.

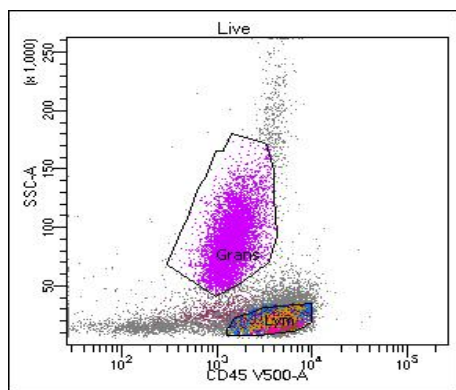


Figure 2: Live cells gated by CD45

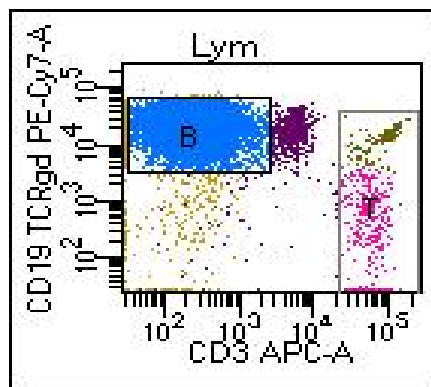


Figure 3: Lymphocytes gated by CD3 and CD19

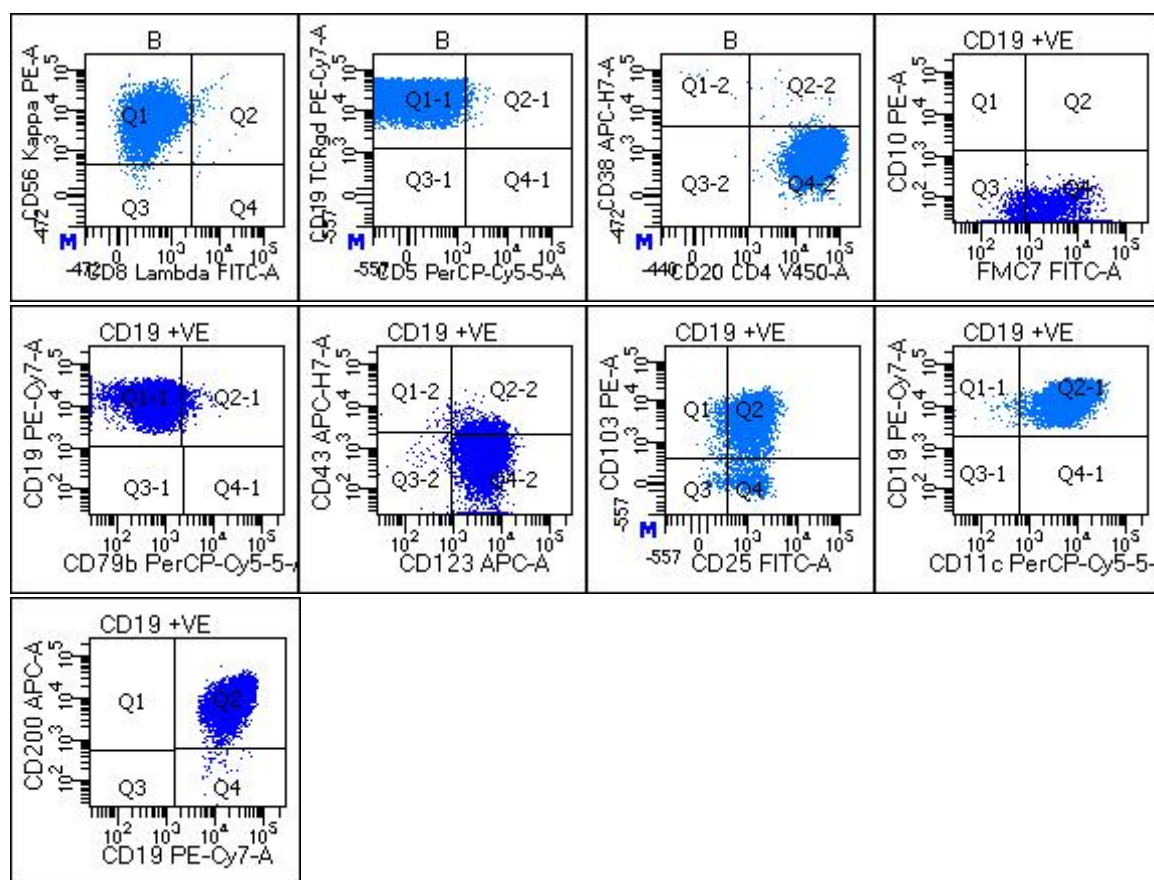


Figure 4: Immunophenotyping of B Lymphocytes

Case report 2

This report was of a 55 year old male patient. He was admitted to the Sri Jayewardenepura General Hospital, Colombo, Sri Lanka with a splenomegaly and absolute lymphocytosis. There was no lymphadenopathy. FBC and immunophenotyping by flowcytometry were requested. The FBC revealed hemoglobin level of 15.2 g/dL, thrombocytopenia ($88 \times 10^3/\mu\text{L}$), and leukocytosis ($15.59 \times 10^3/\mu\text{L}$). Differential count revealed the presence of 12.97×10^3 lymphocytes/ μL (83.2%) with monocytopenia $0.19 \times 10^3/\mu\text{L}$ (1.2%).

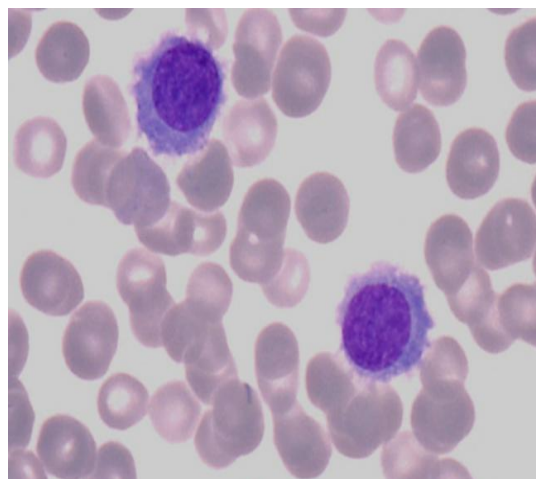


Figure 5: Morphology of peripheral blood

Many atypical lymphoid cells characterized by medium to large cells with some degree of hairy projections were noted in the stained blood film (Figure 5). There were cells with abundant, moderately basophilic cytoplasm and visible nucleoli.

Live cells were gated by CD45 (Figure 6) and two distinct populations as lymphocytes and granulocytes were identified. Lymphocytes were gated by CD3 and CD19 (Figure 7).

Immunophenotyping of peripheral blood showed 83.3% of B lymphocytes with positivity for CD19, monoclonal smIg Kappa, CD103, CD11c and CD20 but, negative for SmIg Lambda, CD5, CD23, CD25, CD38, CD43, CD123, CD79b and CD200 which are typical for HCL-v (Figure 8). However, the CD10 positivity was atypical. The bone marrow was not evaluated. BRAF V600E mutation was negative.

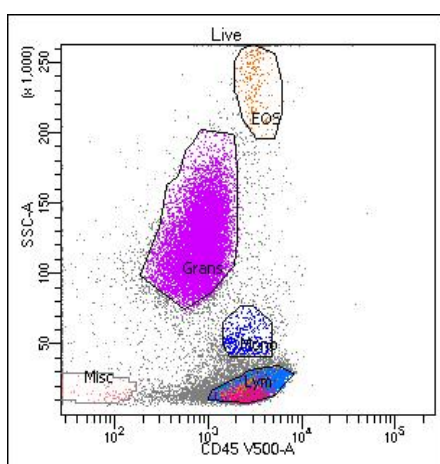


Figure 6: Live cells gated by CD45

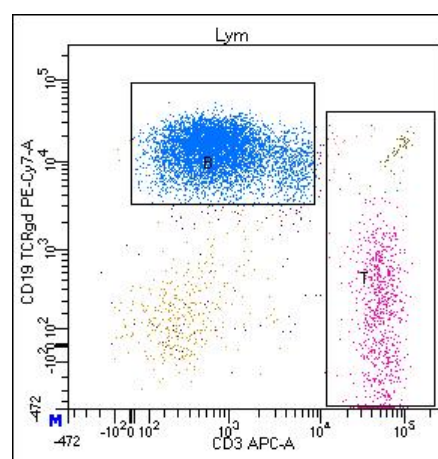


Figure 7: Lymphocytes gated by CD3 and CD19

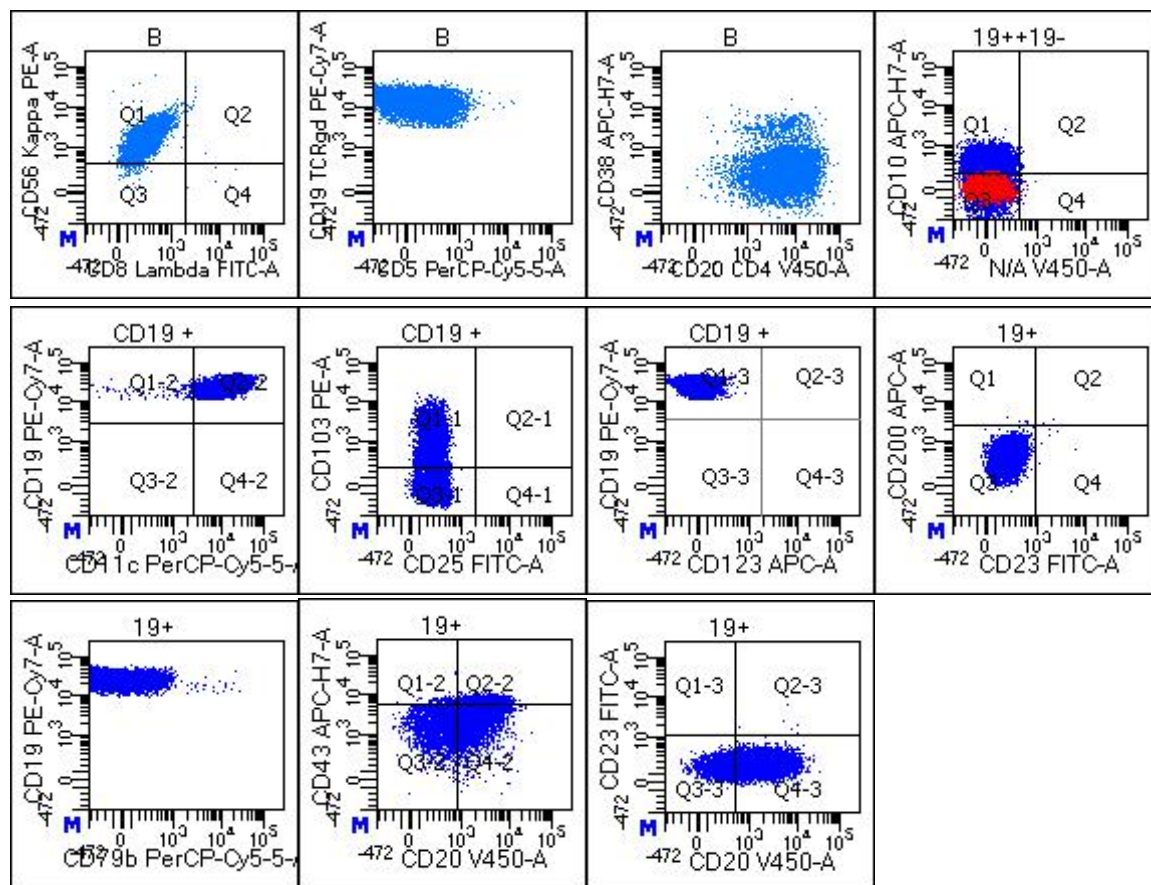


Figure 8: Immunophenotyping of B Lymphocytes

Discussion

HCL is a rare condition occurring in B lymphocytes. Children are very rarely affected [7]. HCL has been identified with a male to female ratio of 5:1 [8]. In this study, 15 year old male patient presenting HCL (Case 1) is considered as a very rare case. According to the World Health Organization, CD5 and CD10 are negative in a group of mature B-cell neoplasms which represent a diverse group. This group includes Diffuse Large B Cell Lymphoma (DLBCL), Marginal Zone Lymphoma (MZL), HCL, Lympho Plasmacytic Lymphoma (LPL), CD10 negative Follicular Lymphoma (FL), and CD5 negative Mantle Cell Lymphoma (MCL). Both cHCL and HCL-v are categorized under CD5-/CD10- group. However, CD10 can be positive in 10-20 % cases of HCL-v [9].

In Case 2, there was a positive CD10 expression, with negative expressions of CD5, C25, CD123 and CD200 characteristic for HCL-v. It has been revealed that increasing polyclonal IgG was reported in four cases of HCL [10] and was seen in Case 1 as well. Though V600E mutation of the BRAF gene can be described as a molecular marker of HCL, BRAF V600E mutation has not been documented in HCL-v. Wildtype BRAF are resistant to conventional HCL therapy especially showing lack of response to cladribine [1,11].

Conclusions

The findings of Case 1 were consistent with a diagnosis of cHCL which was very uncommon at the age of 15 years. The findings of Case 2 were consistent with a diagnosis of HCL-v, despite

having CD10 positivity and monocytopenia.

References

1. Swerdlow, S.H., Campo, E., Harris, N.L., Jaffe, E.S., Pileri, S.A., Stein, H., et al WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4ed. 2017:226-231.
2. Dores, G.M., Matsuno, R.K., Weisenburger, D.D., Rosenberg, P.S. and Anderson, W.F. Hairy cell leukaemia: a heterogeneous disease? *British Journal Haematology*. 2008;142: 45-51.
3. Gupta, A.K., Sachdeva, M.U.S., Ahluwalia, J., Das, R., Naseem, S., Sharma, P., et al. Haematological profile of 21 patients with hairy cell leukaemia in a tertiary care centre of north India. *Indian Journal of Medicine*. 2015;142(4): 426-429.
4. Craig, F.E. and Foon, K.A. Flow cytometric immunophenotyping for hematologic neoplasms, *The American Society of Hematology*. 2008;111: 3942-3966.
5. Arcaini, L., Zibellini, S., Boveri, E., Riboni, S., Rattotti S., Varettoni, M., et al, The BRAF V600E mutation in hairy cell leukemia and other mature B-cell neoplasms, *Blood journal*. 2012;119: 188-191.
6. Morton, L.M., Wang, S.S., Devesa, S.S., Hartge, P., Wisenburger, D.D. and Linet M.S. Lymphoma incidence patterns by WHO subtype in the United States, 1992–2001, *Blood*. 2006;107: 265-276.
7. Bosma, M. and Bartels, M. Hairy cell leukemia in a child? *Blood*. 2018: 132:1216.
8. Dores, G.M., Matsuno, R.K. and Weisenburger, D.D. Hairy cell leukaemia: a Hairy Cell Leukemia Workup Updated: 2018.
9. Gorczyca, W. Flow cytometry in neoplastic hematology morphologic immunophenotypic correlation. 2010; 2nd ed: 136-197.
10. Keren, D.F. Protein Electrophoresis in clinical diagnosis, Taylor and Fransis group. 2003;133.
11. Getta, B., Wahab, O.A., Park, J.H. and Tallman, S.M. Cytogenetics in Hairy Cell Leukemia at Diagnosis and Relapse: The Rate of Therapy-Related Myeloid Malignancies Is Low, *American Society of Hematology*. 2015;126: 2644.