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Hairy Cell Leukemia-Variant

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Abstract:- Hairy cell leukemia variant (HCLv) / Splenic B cell-lymphoma/leukemia with prominent nucleoli (SBLPN) is a more aggressive disease, refractory to standard therapy. Molecular evaluation does not reveal BRAFp.V600E mutation unlike classic HCL.

Keywords:- *Hairy Cell Leukemia, Splenic B Cell-Lymphoma/Leukemia with Prominent Nucleoli, Hclv, BRAF.*

I. INTRODUCTION

Hairy cell leukemia variant (HCLv), is now called Splenic B cell-lymphoma/leukemia with prominent nucleoli (SBLPN) as per the WHO classification of haematolymphoid tumors (5th edition)[1]. It is morphologically characterized by atypical lymphoid cells in the peripheral blood, bone marrow and spleen and is clinically associated with splenomegaly. These cells have abundant cytoplasm with hairy projections. It varies from the classical hairy cell leukemia by the presence of leucocytosis without monocytopenia, cells having prominent nucleoli, negative hairy cell markers (CD25 and CD123) on flow cytometry and lack of BRAFp.V600E mutation. Awareness of this entity is important due to its aggressive behavior and non-response to standard therapy used for the classical hairy cell leukemia.

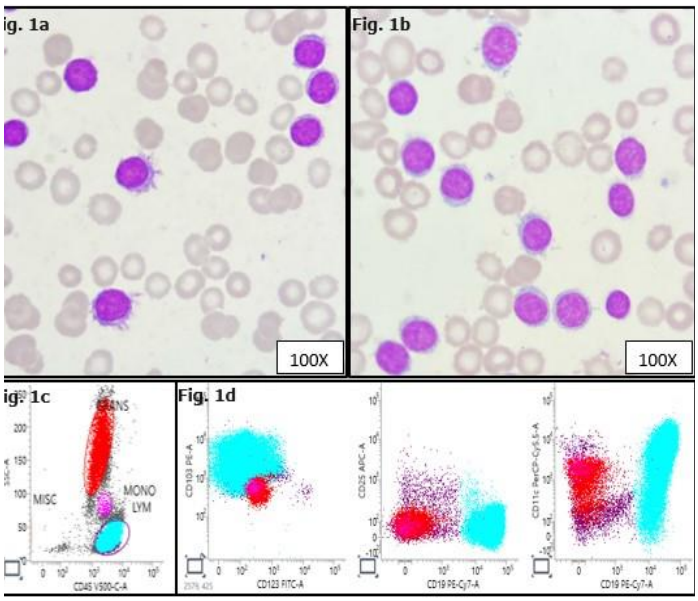
II. CASE REPORT

We present a 74-year-old female who came to our hemato- oncology department with complaints of generalised weakness, reduced oral intake and weight loss. On examination, she had splenomegaly with leucocytosis (209910 / cu mm). Peripheral smear (Fig. 1a and 1b) showed 70% atypical, small to medium sized lymphoid cells having hairy cytoplasmic projections. This led us to process the sample for immunophenotyping by flow cytometry (Fig. 1c and 1d) which revealed 90% monotypic (kappa restricted) CD5 and CD10 negative B cells (aqua blue). This population of cells expressed pan-B cell markers (CD19, CD20, FMC7, CD79b) and was negative for T/NK cell markers (CD3, CD7, CD4, CD8, CD56). In view of the morphology, we added confirmatory markers for hairy cell leukemia. The cells were positive for 2 of these 4 markers i.e. CD103 and CD11c but negative for CD25 and CD123. The other laboratory parameters are detailed in Table1. Bone marrow study was not done. We completed the work-up with BRAFp.V600E mutation analysis, which was not detected by RT-PCR method. We concluded this case as Hairy cell leukemia-variant.

Not many cells had a conspicuous nucleolus in our case, hence based on the complete work-up, we ruled out the other differential diagnoses of classic hairy cell leukaemia, splenic marginal zone lymphoma and splenic diffuse red pulp lymphoma and labelled this case as HCLv/SBLPN.

Our patient was given Rituximab to start with. However, she developed severe infusion reactions with the first dose in the form of fever, chills, respiratory distress and desaturation. In view of respiratory distress, she was started on non-invasive ventilation. Treatment was then changed to Cyclophosphamide, which she tolerated well. However, she subsequently developed pneumonia and had to be treated with broad spectrum antibiotics. Her clinical condition deteriorated and she landed up in septic shock. Despite aggressive management, she succumbed to cardio respiratory arrest.

A. Figures



1. Peripheral smear (Fig. 1a and 1b) – showing atypical lymphoid cells with hairy projections
2. Flow cytometry scatterplots (Fig. 1c and 1d) revealed 90% B lymphoid cells positive for 2 of the 4 hairy cell markers i.e. CD103 and CD11c but negative for CD25 and CD123

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III. DISCUSSION

In a study by E. A. Angelova et al[3]. consisting of 23 patients with hairy cell leukemia including variants, splenomegaly was detected in 19 (90%) patients similar to the presentation in our case. However, they also found lymphadenopathy in 33% patients, often involving abdominal or retroperitoneal nodes and hepatomegaly in 28% patients. Even morphologically, only 12 of their 23 cases actually had a prominent nucleolus, while the rest had either inconspicuous or no nucleolus at all. One should note that though WHO has used Splenic B-cell Lymphoma with "Prominent Nucleoli" as the newer terminology for this variant, one should be aware that prominent nucleoli may not be a reliable feature as in our case.

The immunophenotype of the HCLv is very classic. In the study done in Japan, reported by Machii T et al[4]., only 9 cases were of classical HCL, 2 cases were of the HCL prolymphocytic variant and the remainder were of the so called "HCL-Japanese variant", as they frequently presented with a high WBC count and with a distinct CD25 negative population with hairy morphology. Pankaj Pande et al[5], also reported atypical lymphoid cells to be negative for CD 25 but positive for CD11c, CD19, CD20, CD22, FMC7, HLA-DR, SmIgD and the kappa light chain. Our case was also CD25 negative on flow cytometry.

Study by E. A. Angelova et al[3] revealed that the HCLv cases were negative for 600E mutations which is one of the diagnostic criteria for Hairy cell leukemia variant according to WHO hematolymphoid neoplasms 5th Edition[1]. It is known that HCLv is more aggressive and does not respond to the standard treatment of classical hairy cell leukemia. A study from Memorial Sloan Kettering reported that HCLv patients had shorter time to next treatment than patients with classic hairy cell leukemia, but had a similar overall survival (median follow-up was 47 months). In addition, recent report suggests that treatment with anti-CD22 immunotoxins, anti-CD52 antibody (Alemtuzumab), Fludarabine, or Ibrutinib is effective in HCLv and these agents need further investigation. In our case we presume that since the disease burden was more the patient did not tolerate even the single dose of Rituximab.

IV. CONCLUSION

In summary, patients with Hairy cell leukemia variant can exhibit a varied spectrum of clinical, morphologic, immunophenotypic and genetic features. Diagnosis of hairy cell leukemia variant is frequently a challenge. It is important to correctly identify this variant as it has a more aggressive course and is refractory to standard therapy[2]. Evaluation of immunophenotype by flow cytometry and / or immunohistochemistry and mutation analysis (BRAFp.V600E) are useful tools in distinguishing hairy cell leukemia variant form other small B cell lymphomas.

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Table 1 Laboratory Parameters

Hematological parameters			Biochemical parameters		
Test parameter	**Value**	**Reference range and units**	**Test parameter**	**Value**	**Reference range and units**
Hemoglobin	4.6	12 – 15 g/dL	A:G Ratio	1.80	1.1 - 1.8 :1
RBC Count	1.24	3.8 - 4.8 million/cu mm	Albumin	3.6	3.5 - 5.2 g/dL
PCV	14.0	36 - 46 %	Alkaline Phosphatase (ALP)	147	35 - 104 U/L
MCV	112.9	77 - 95 fl	ALT (SGPT	14	0 - 33 U/L
MCH	37.1	27 - 32 pg	AST (SGOT))	26	0 - 35 U/L
MCHC	32.9	31.5 - 34.5 g/dL	Direct Bilirubin	0.59	0 - 0.3 mg/dL
RDW CV	23.6	11.6 - 14 %	Total Bilirubin	1.4	Upto 1.2 mg/dL
Total Count	209910	4000 - 10000 /cu mm	Gamma GT	22	6 - 42 U/L
Platelet	42000	150000 - 410000 /cu mm	Globulin	2.0	2.5 - 3.5 g/dL
Absolute lymphocyte count	181820	1000 – 3000 /cu mm	Total Protein	5.6	6.6 - 8.7 g/dL
Neutrophils	19.9	40 - 70 %	Creatinine	0.71	0.5 - 0.9 mg/dL
Lymphocytes	76.6	20 - 40 %	LDH	246	135 - 214 U/L
Monocytes	3.1	2 - 10 %	Magnesium	2.06	1.3 - 2.14 mg/dL
Eosinophils	0.3	1 - 6 %	Potassium	4.7	3.5 - 5.5 mEq/L
Basophils	0.1	<1 - 2 %	Phosphorus	3.3	2.5 - 4.5 mg/dL