Case Report

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Hairy Projections on Non Hairy Cells- A Case Report

Pathology Section

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ABSTRACT

Adult T-Cell Leukaemia/Lymphoma (ATLL) is a mature T-cell neoplasm. It is caused by human retrovirus Human T-cell Lymphotropic Virus Type 1(HTLV-1). The neoplastic cells after monoclonal integration begin to express T-cell associated antigens namely CD2, CD3 and CD5. These leukaemic cells are highly pleomorphic in light microscopic appearance and also they have a highly variable clinical presentation ranging from acute to lymphomatous to chronic to smouldering. There is a chance of missed or miss diagnosis due to their morphological and clinical heterogeneity and specialised test like immunophenotyping or flow cytometry is essential for exact categorisation. Authors hereby, report a case of 45-year-old female patient suffering from ATLL whose peripheral smear showed leukaemic cells with unusual hairy projections resembling hairy cell leukaemia posing diagnostic dilemma.

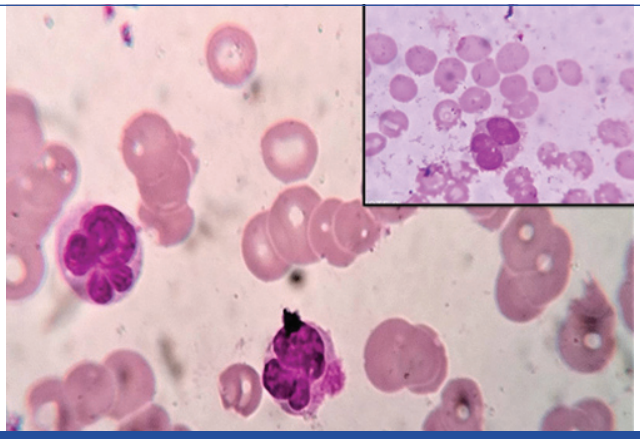
Keywords: Adult T-cell leukaemia, Hair like projections, Light microscopy

CASE REPORT

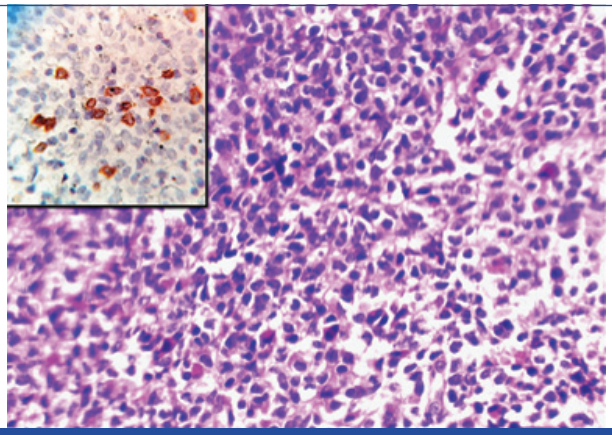
A 45-year-old female of Indian ethnicity presented to the Medicine Outpatient Department with three months history of abdominal pain in left upper quadrant, which was followed by abdominal distension since last one month. She also complained of generalised weakness and dry cough for same duration. Later, she developed oliguria, nausea, vomiting, muscle cramps and respiratory distress. On general examination, she had pallor and her respiratory rate was 30/min. On systemic examination, there were basal crepitations in one lung field and shifting dullness of abdomen. Mild hepatosplenomegaly was also noted. There was no lymphadenopathy or any visible skin lesions. Laboratory parameters revealed haemoglobin 8.12 g/dL, leukocytosis with total leukocytes count of 54×10^9/L and reduced platelet count of 80×10^9/L. Serum uric acid was 14.3 g/dL, serum potassium 4.0 mEq/L, serum phosphate 3.8 mg/dL, serum calcium 10.7 mg/dL urea 48 mg/dL, creatinine 1.1 mg/dL, serum Lactate Dehydrogenase (LDH) 856 U/l. High resolution computed topography thorax was performed which revealed a thin pleura-parenchymal fibrotic bands in right upper lobe suggestive of an infective lesion. Ultrasonography whole abdomen revealed mild hepatomegaly and mild splenomegaly. Contrast enhanced computed tomography whole abdomen showed gross ascites.

Peripheral smear examination revealed 62% atypical mononuclear cells which were medium in size with pale blue cytoplasm and bilobed to multilobed nuclei with prominent nucleoli. These resembled “flower cells” morphologically [Table/Fig-1].

Bone marrow aspiration and biopsy was performed from the posterior superior iliac spine. Bone marrow aspiration was found to be a particulate, but imprint smears revealed hypercellularity. Erythropoiesis and myelopoiesis were depressed. There was presence of 43% atypical mononuclear cells. Cells were medium in size with basophilic cytoplasm and unusual polar and few circumferential hair like projections [Table/Fig-1]. Nuclei show bilobation, multilobation and polylobation resulting in the formation of flower cells. Chromatin was open with presence of nucleoli [1,2]. Megakaryocytes were markedly depressed in number and only identified in imprint smears. Mitosis was found to be increased. In view of presence of flower cells both in peripheral smear and bone marrow aspirate, possibility of ATCL remained strong. However, hairy cell leukaemia was the closest differential diagnosis. Next the bone marrow biopsy revealed scattered haematopoietic precursors intermixed with blasts [Table/Fig-2]. Immunohistochemical staining was done on paraffin embedded block which showed weak expression for CD3 [Table/Fig-2]. Further immunophenotyping was done and the result corroborated with ATLL. These cells expressed cytoplasmic CD3, CD2, CD5, Terminal deoxynucleotidyl Transferase (TdT) and Myeloperoxidase (MPO), CD19, CD10, CD11c, and CD64 were found to be negative. However, HTLV-1 antibody testing by Western Blot or Enzyme-Linked Immuno Sorbent Assay (ELISA) could not be performed due to lack of resources. The patient was subsequently referred to specialised centre treating haematological malignancies.



[Table/Fig-1]: Peripheral blood smear shows medium sized cells with pale blue cytoplasm and multilobated nuclei resembling flower cells (100x). Inset shows hair like projections (Leishman stain, 1000x).



[Table/Fig-2]: Bone marrow biopsy shows hematopoietic precursors intermixed with blasts. (H&E, 400X) Inset shows weak cytoplasmic CD3 expression.

DISCUSSION

Adult T-Cell Leukaemia/Lymphoma (ATLL) is a mature T-cell neoplasm caused by human retrovirus HTLV-1. It is well known for its diversity in clinical presentation ranging from favourable chronic to unfavourable acute variants involving blood and bone marrow [1]. Presence of blast cells with petal like nuclei and coarse chromatin pattern (flower cells) gives the initial morphological suspicion although the number varies depending on the clinical stage. But unusual hairy projection on cell surface is rarely reported [2]. Here is a case report of ATLL which on light microscopic examination revealed fine hairy projection on cell surface resulting in diagnostic difficulty with hairy cell leukaemia which is a B-cell neoplasm. Knowledge about this morphological mimicry is essential to prevent missed or miss diagnosis during initial evaluation and to guide to effective utilisation of specialised tests.

The cytoskeleton is composed of proteins that give the cell shape and internal organisation. They help the cell to adopt a particular shape, maintain polarity, organise the intracellular contents or migrate to other sites. In eukaryotes, the three major cytoskeleton proteins are actin, intermediate filaments and microtubules [3]. Hairiness is nothing but cellular projections composed of actin molecules.

In hairy cell leukaemia cells, the cortical cytoskeleton is composed of polymerised actin (F-actin). These support the Filamentous (F) membrane projections on hairy cell leukaemia cells. In contrast, normal B cells and in B-cell chronic lymphocytic leukaemia cells, F-actin is primarily located in the central part of the cell [4]. Thus, cells in hairy cell leukaemia increase the concentration of actin at the periphery to hold their membrane projections.

Earlier, it was thought that the presence of hairy projections were a hallmark for hairy cell leukaemia. This was thought to be a result of BRAF mutation which was a constantly present in all hairy cell leukaemia cells. However, the presence of hairy projections on non-hairy cells and the absence of BRAF mutations in them refuted this fact [4]. Hairiness on non-hairy cells was thus thought to be an adaptation of leukaemic cells to increase the surface area to enhance cellular fitness in their microenvironment. Viral and bacterial pathogens may also induce reorganisation of the cytoskeleton structure of the host cell as a part of cytopathic effect and thus develop means to evade the humoural immune response [4].

Hairy projection on cells opened the door to many differentials. Hairy cell leukaemia topped the list followed by variants of hairy cells, splenic diffuse red pulp lymphoma and splenic marginal zone lymphoma. Again, Tanioka F et al., reported the presence of hairy cell morphology in a case of primary plasma cell leukaemia [5]. Similarly, Ahluwalia J and Sachdeva MU, noted hairy projections in a case of hepatosplenic T-Cell non Hodgkin lymphoma [6]. Somasundaram V et al., reported a case of circumferential hairy projections in T-ALL [2]. Literature points to the co-existence of hairy cell leukaemia in various haematological malignancies as Hodgkin lymphoma, peripheral T-Cell lymphoma, multiple myeloma, chronic myeloid leukaemia and chronic lymphocytic leukaemia.

Distinguishing hairy cell leukaemia from ATLL based on immunophenotyping was of paramount importance considering the fact that hairy cell leukaemia responded well to purine analogues and had a good prognosis. In contrast, Adult T-cell has a poor prognosis and treatment depended upon clinical subtypes. The standard treatment proposed as first line was zidovudine (AZT) and Interferon-α (IFN-α). Chemotherapy was proposed only for lymphoma form. Further, patients with the smouldering and favourable chronic forms are not submitted to specific treatments. Here, narrow band ultraviolet B phototherapy is used for more superficial lesions and psoralen and ultraviolet A for more infiltrated lesions. Also, phototherapy combined with etoposide was a new treatment regimen proposed [7].

Present case also outstood in this category of non-hairy cells with projections enough to cause a diagnostic dilemma. However, in contrast to long thin circumferential projections on hairy cells, our case had few polar and few circumferential short tuft like projections. Also, further immunophenotyping with mature T-cell markers expression markers usually CD2, CD5, HLA-DR and TCR αβ positive with aberrant loss of CD7 and CD3 negative/dim confirmed the diagnosis of ATLL.

CONCLUSION(S)

The ATLL should be kept in mind while evaluating peripheral blood smears with atypical cells showing hairy projections. A high index of clinical suspicion and ancillary tests like immunophenotyping help in reducing the number of miss or missed diagnosis.

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