Immunophenotypic Aberrancy of a Case of Hairy Cell Leukemia

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Dear Editor,

Hairy cell leukemia (HCL) is an uncommon but distinct form of chronic B cell lymphoproliferative disorder, comprising about two percent of lymphoid leukemias. The pathologic diagnosis of HCL is based mainly on morphology and immunophenotype leukemic cells. HCL has a characteristic immunophenotypic profile and light scatter characteristics. The tumor cells express B cell-associated markers, CD19, CD20, CD22, and CD79b, and are characteristically positive for CD103, CD11c, and CD25 and usually negative for CD10, CD5, and CD23 [1]. However, atypical immunophenotypes have been reported in otherwise typical HCL [2–5]. We report a case of HCL which had usual clinical and morphological findings, however

expressed several unusual aberrant immunophenotypic markers.

A 32 year old male presented with 2 month history of weakness and awareness of mass in left upper side of abdomen. On examination, he had pallor and palpable spleen 20 cms below left costal margin, however, there was no icterus, lymphadenopathy or hepatomegaly. Other systemic examination was within normal limits. Laboratory parameters revealed haemoglobin, total leucocyte count and platelet count of 10.7 gm/dl, 27×10^3 and 45×10^3 /cumm respectively. Peripheral smear examination revealed 72 % of mononuclear cells with abundant cytoplasm and circumferential hairy projections which were positive for TRAP staining. Flowcytometric immunophenotyping (Fig. 1) revealed features characteristic of HCL, that is, positivity for CD19, CD11C, CD25 and CD103. In addition, these CD19 positive cells showed co-expression of CD5, CD 10 and CD 2 while negative for CD3 and CD23. Further these cells were positive for CD20, CD200, FMC7 along with lambda light chain restriction. Subsequent bone marrow examination revealed infiltration by hairy cells with characteristic ‘fried egg’ appearance in bone marrow biopsy.

With final diagnosis of HCL, patient was treated with cladribine @ 0.09 mg/kg for 7 days with prophylactic cotrimoxazole, fluconazole, and aciclovir from admission till discharge. The patient tolerated chemotherapy well without infusional reactions, however was started on G- CSF from day 9 of therapy. His spleen size regressed to two cms below costal margin. Patient is presently in complete hematological remission (CR) for past 3 months.

Aberrant expression of T-cell-associated antigens on B cell non-Hodgkin lymphomas (NHLs) other than CD43 is a known but uncommonly observed phenomenon. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) is the most cited B-cell malignant neoplasm with

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Fig. 1 Flow cytometry dot plots showing that the neoplastic B-cells co-express CD11c, CD25, CD103 with lambda light chain restriction. The cells also express FMC7, CD2, CD5 and CD 10

aberrant coexpression of T-cell-associated antigens [6]. Hairy cell leukemia (HCL) exhibits a characteristic immunophenotypic profile that is strongly positive for pan-B-cell markers and positivity for CD103, CD11c, and CD25; and usually negative for CD5, CD10, and CD2. The present case revealed aberrant expression of all these three markers which is extremely unusual in HCL.

Chen et al. [7] evaluated 35 HCL cases and identified CD10 expression which is a marker for B-cell neoplasms of follicular center origin in five (14 %) cases. The frequencies of CD10 expression in HCL in the reported studies ranged from 5 to 26 % [5]. CD2 and CD5 have been shown to be rarely expressed in HCL cases. Of 169 cases of typical HCL evaluated by Shao H et al. three cases (2 %) showed expression of CD2 and four cases (2 %) showed expression of CD5 respectively. However the expression of CD 2 is more often seen in HCL variant cases to the tune of nine percent. Occurrence of a second concurrent monoclonal B cell population is mentioned in the same study with the second clone exhibiting a CLL/non specific IPT features. The light chain expression between the two monoclonal B-cell populations was different in all

three patients, indicating different clonal origins of the two populations [8]. However in our case it was a single clonal population ruling out a second clone which is responsible for expression of CD2, CD5 and CD10.

As far as minimal residual disease (MRD) detection in HCL is concerned flowcytometry is more sensitive and more specific and it also permits quantitation of tumor cell number [9]. Hence, the valuable information of this aberrant leukemia associated immunophenotype (LAIP) expressed in HCL cases adds more specificity in MRD analysis. In a resource limited setting, application of minimal antibody panel for diagnosis of lymphoma/leukemia by flowcytometry would result in non identification and under reporting of valuable information such as aberrant antigen expression. This information will not only aid in correct diagnosis of cases but also will aid during follow up in the form of MRD analysis. Also use of a limited antibody panel may result in misdiagnosis in select cases, due to aberrant antigen expression.

Hence this communication indicates that it is not uncommon for HCL to display an unusual immunophenotype. Recognition of the variability of immunophenotype

and correlating with morphologic and clinical features are essential for establishing an accurate diagnosis of HCL. The distinction between HCL and other chronic B-cell lymphoproliferative disorders is clinically important because patients with HCL do not respond well to conventional lymphoma chemotherapy but are highly sensitive to purine analogues such as cladribine (2-chlorodeoxyadenosine) and pentostatin (2'-deoxycoformycin). Further, even though the HCL may show immunophenotypic aberrations, the outcome of these cases are comparable with those exhibiting the usual IPT features as brought by Chen et al. [7]. The present case also responded well and is in remission for the past 3 months following therapy with cladribine.

The Manuscript has been approved by the Institute's ethics committee and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

A written informed consent was obtained from the patient prior to the procedures and treatment. Details that might disclose the identity of the subjects under study have been omitted.

Conflict of interest None.

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