

# Lymphoma without Lymphadenopathy

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A seventy-five years old man was presented to our hospital with a complaint of gradually progressive heaviness in the left half of abdomen for past 10 months. History was negative for fever, weight loss, and night sweats. Physical examination was noteworthy for moderate pallor and massive splenomegaly [Figure 1a].

There was no lymphadenopathy. Routine investigations showed: Hemoglobin 70 g/L, total leucocyte count:  $98.4 \times 10^9/L$ , neutrophils: 4%, lymphocytes: 93%, monocytes: 2%, and platelet count:  $103 \times 10^9/L$ . Peripheral blood smear showed markedly increased the number of leukocytes with a fair number of smudged cells. Red blood cells showed anisopoikilocytosis with the predominantly normocytic normochromic picture [Figure 1b].

Platelets were reduced in number to  $103 \times 10^9/L$ . Renal and liver function tests, serum lactate dehydrogenase (298 U/L), serum uric acid levels (6.5 mg/dl), chest X-ray, and electrocardiogram were within normal limits. Coomb's test was negative, and stool analysis was negative for occult blood. The ultrasonography of abdomen showed gross splenomegaly [Figure 1c]. Contrast-enhanced computed tomography (CT) of chest and abdomen confirmed splenomegaly and did not reveal additional information. However, positron emission tomography-CT imaging was not performed.

Conventional karyotyping was normal. The patient did not give consent for splenic aspiration. Bone marrow aspiration and biopsy revealed diffuse infiltrates of small lymphoid cells with nuclear round contour and scanty cytoplasm, suggestive of chronic lymphocytic leukemia (CLL) [Figure 2a]. Immunophenotyping by flow cytometry revealed: CD79b (77.1%) was strongly positive, CD5 (98.1% of gated lymphocytes), and

CD23 (51.1%) were positive. FMC-7 was positive (51.1%), and surface immunoglobulin (1.7%) was negative. Immunophenotyping results were disfavoring CLL/small lymphocytic lymphoma (CLL/SLL) as according to the scoring system, a score of 4 or 5 is required for the diagnosis of CLL, whereas here the score was 3.

Typically, CLL cells express weak monotypic surface immunoglobulin, CD5, CD19, CD23 and weak or absent CD79B, CD22, and FMC7. Using a recommended panel of scoring system for the diagnosis of CLL.<sup>[1]</sup> Ninety-two percent of CLL cases score 4 or 5, 6% score 3, and 2% score 1 or 2. Most other chronic B-cell lymphomas and leukemias score 1 or 2, but a minority score 3. Scores in CLL are usually  $>3$ , in other B-cell malignancies the scores are usually  $<3$ .

The scatter parameters and antigen expression profile as studied by flow cytometry of the sample were suggestive of atypical chronic lymphocytic leukemia, B-CLL. No single type of lymphoma/leukemia was matching with clinical and flow cytometry parameters.

In spite of the absence of lymphadenopathy, presence of massive splenomegaly and lack of "CD23 negativity" mantle cell lymphoma (MCL) was a possibility before labeling it as atypical B-cell CLL, as there are case reports of MCL without lymphadenopathy and with CD23 positivity, but the combination of all three parameters (absence of lymphadenopathy, presence of massive splenomegaly, and CD23 positivity) were making possibility of MCL dubious.

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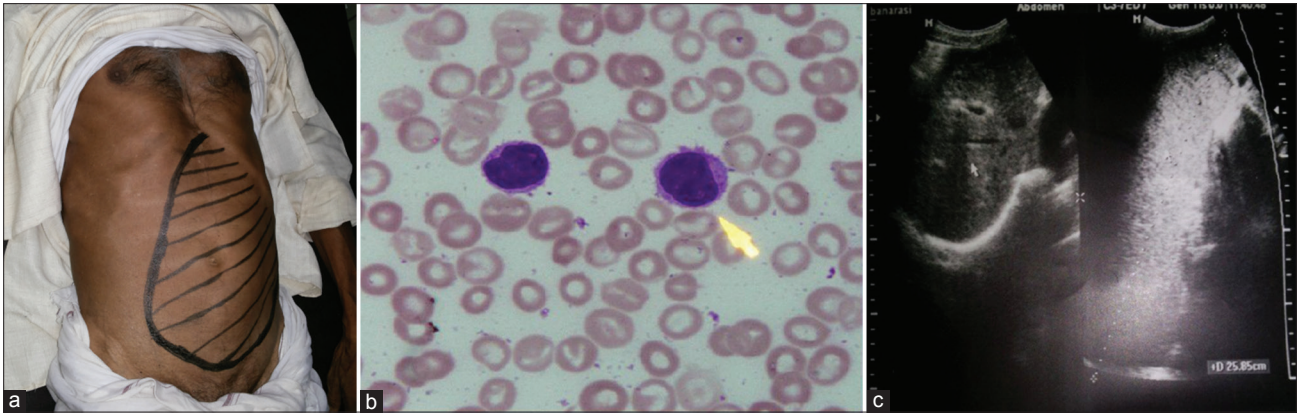
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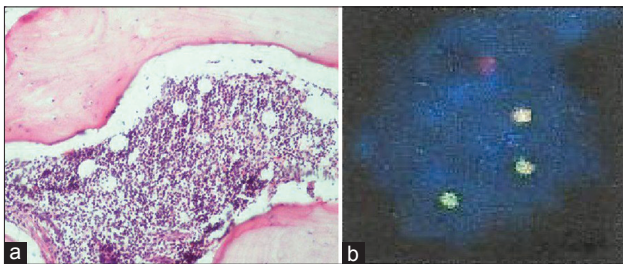


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**Figure 1:** Splenic area marked (a); Peripheral blood film (b); Ultrasonography showing splenomegaly (c).



**Figure 2:** Bone marrow trephine biopsy (a); Fluorescence *in situ* hybridization was done, and it was positive for IgH/CCND1 fusion signal (b).

But flow cytometry results prompted us to pursue the diagnosis of MCL as it was the only other plausibility apart from CLL, for which flow results were least unfavorable.

Fluorescence *in situ* hybridization (FISH) was done, and it was positive for IgH/CCND1 fusion signal. IgH/CCND1 fusion signal was detected in 92% cells by FISH [Figure 2b].

MCL is one of the several subtypes of B-cell non-Hodgkin lymphoma. The distinction between SLL/CLL and MCL has important clinical implications. Typically, SLL/CLL is CD23+, whereas MCL is CD23-. The majority of MCL cases co-express CD20, CD5, BCL2, and cyclin D1. MCL is usually negative for CD10, BCL6 and CD23. Chromosomal translocation characteristic for MCL is t(11;14)(q13;q32), which results in overexpression of the cell cycle protein cyclin D1.<sup>[2]</sup>

In reports that include CD23+ MCL cases, detected by flow cytometric or immunohistochemical analysis, the frequency

of CD23 expression has ranged from 2% to 45%. MCL is an aggressive lymphoma with moderate chemosensitivity. Reliably curative treatments for MCL are lacking. An inexorable pattern of progression is characteristic, with a median time to treatment failure of <18 months.<sup>[3,4]</sup>

The absence of lymphadenopathy and presence of CD23 positivity makes this case a rare one among all MCL cases. This patient was started on bendamustine rituximab chemoregimen for 6 cycles, and he showed partial remission after completion of the fourth cycle.

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#### Conflicts of interest

There are no conflicts of interest.

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