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SPURIOUS LEUKOCYTOSIS LEADS TO A DIAGNOSIS

Pathology

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ABSTRACT

Fifty years old female presented with cervical lymphadenopathy, headache, and weight loss for 2 weeks. On examination, she had purpuric spots. Investigations revealed erroneous counts revealing interference by cryoglobulin. Lymphoplasmacytic lymphoma was suspected because of cryoglobulin interference, purpuric spots, and lymphadenopathy. The lymph node showed atypical small lymphocytes admixed with plasma cells. The cells were positive for CD45, CD20, CD79a, PAX-5, MUM-1 & Kappa confirmed the diagnosis. Careful evaluation of histogram and scatterogram in a patient with leukocytosis indicated interference by cryoglobulin, which leads to further investigation. The pathologist is responsible for differentiating spurious leukocytosis from leukocytosis so the underlying condition can be diagnosed and managed.

KEYWORDS

Lymphoplasmacytic lymphoma, Cryoglobulins, Scatterogram.

INTRODUCTION:

Spurious blood cell counts occur due to preanalytical errors and interfering substances in the plasma, like antibodies, cryoglobulins, and many more. The automated hematology analyzer generates histogram and scatterogram, which, when analyzed carefully, helps differentiate actual counts from spurious ones. This differentiation is essential as the interfering substances may be products of neoplasms. The blood count may be a guiding tool to diagnose a disease.

Case Presentation:

A 50-year-old postmenopausal woman, presented with single swelling in the neck, weight loss and headache, for 2 weeks. The patient was pale on general examination, and a single cervical lymph node measuring 2.5x1 cm in size and firm consistency was observed. Rosy spots were noted in the arms. Radiological investigations did not reveal any abnormalities. She did not have any comorbid conditions. She is from a middle-class educated family, and has 2 sons. Parents and elder siblings were normal in health.

Investigations:

In view of the purpuric spots, she was admitted with a provisional diagnosis of dengue. Complete blood count with fully automated hematology analyzer revealed: Hemoglobin- 5.9 grams/dl, Total WBC count - 1,68,000 cells/ cu.mm, platelets- 4,70,000/cu.mm.

Test	Result	Flags
WBC	166.0	R c H
UWBC	167.0	R c H
RBC	2.30	R L
HGB	5.9	R c L
HCT	17.9	R c L
MCV	77.9	R L
MCH	25.7	R L
MCHC	33.0	R
RDW	14.3	R
RDW-SD	39.8	R
PLT	470	R H
MPV	9.0	R

Test	Result	Flags
WBC	4.8	
UWBC	4.8	
RBC	2.25	L
HGB	6.0	c L
HCT	17.4	c L
MCV	77.5	L
MCH	26.5	L
MCHC	34.3	
RDW	14.4	
RDW-SD	39.4	
PLT	145	R L
MPV	7.4	R

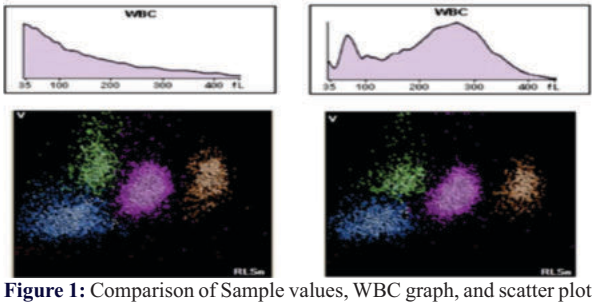

Figure 1: Comparison of Sample values, WBC graph, and scatter plot before and after sample incubation.

The tables and the images on the left side show the flags raised by the analyzer due to the high count, and varied distribution in the white blood cell(WBC) graph and scatter plot, leading to a critical alert. The right side shows the values, WBC, and scatter plot obtained after incubating the sample.

The WBC histogram showed interference before 35 fl. The presence of cryoglobulins was suspected. The fresh sample was incubated at 37o C, which, when processed, showed hemoglobin- 6 gm/dl, a total WBC count of 4,800 cells/cu.mm, and platelets- 1,45,000/cu.mm. The coagulation screen was within normal limits.

In view of the clinical presentation of purpura and lymphadenopathy and the laboratory finding of cryoglobulin, a cervical node excision biopsy was done. The node was 2x1.5x1 cm, firm with a grey-white cut surface. Microscopically paracortical expansion by the spectrum of atypical small lymphocytes, plasmacytoid lymphocytes and plasma cells was noted. By immunohistochemistry, the lymphocytes were positive for CD45, CD20, CD79a, PAX-5, MUM-1 & Kappa. Plasma cells were focally positive for CD-138 & CD20. CD3 & lambda were negative. The Ki-67 labeling index was less than 20%. (Figure 2 and Figure 3)

Serological investigations were negative for dengue, hepatitis B, hepatitis C, Human immunodeficiency virus, and rickettsiae. Serum creatinine(1.9 mg/dL) and LDH(349 U/L) were raised, and other biochemical parameters were within reference range. A bone marrow biopsy was performed, which did not reveal any infiltration by tumor.

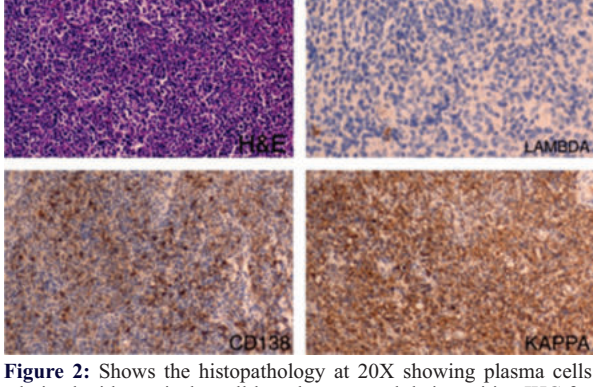

Figure 2: Shows the histopathology at 20X showing plasma cells admixed with atypical small lymphocytes and their positive IHC for CD138 & kappa, negative IHC staining for Lambda at 20X seen.

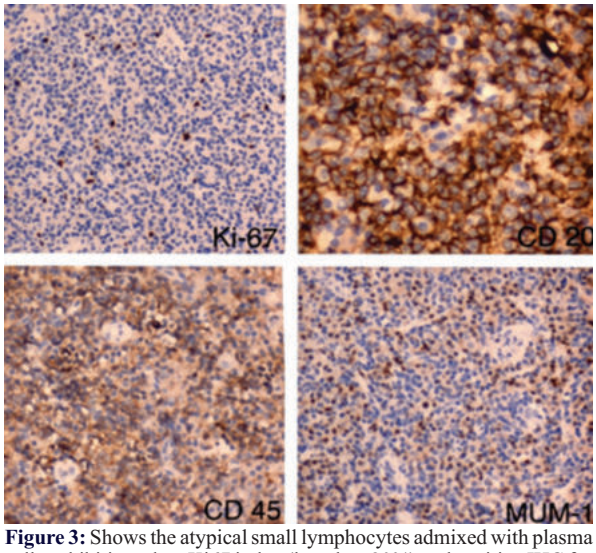

Figure 3: Shows the atypical small lymphocytes admixed with plasma cells exhibiting a low Ki67 index (less than 20%) and positive IHC for CD 20, CD 45 & MUM-1.

Differential Diagnosis:
The presence of headache, lymphadenopathy with purpura, and spurious blood cell counts due to cryoglobulin interference and histopathology picture with immunohistochemistry confirmed Lymphoplasmacytic lymphoma (1,2).

Outcome and Follow-up:
The patient was counseled for treatment but refused and lost to follow-up.

DISCUSSION:

Cryoglobulins are immunoglobulins that precipitate at a temperature of less than 37°C, due to which abnormal counts are observed on the hematology analyser [1,2]. Interference of cryoglobulin leading to erroneous WBC counts had been reported as early as 1973 [1]. If cryoglobulin particles cluster together or if their size is large, the WBC count is spuriously increased. Interference is detected by incubating the sample at 37°C for 30 minutes and reanalysing the Sample [3]. Cryoglobulins are secreted commonly in HCV-associated non-Hodgkin lymphoma. This patient is HCV-negative.

The differential diagnosis includes multiple myeloma, and chronic lymphocytic leukaemia, which have been ruled out by morphology and IHC [4,5]. LPL is a very rare monoclonal gammopathy with an incidence of 3-4 cases per million population. LPL is often associated with paraproteinemias, usually IgM type [6]. 20% of LPL have cryoglobulinemia [4]. Purpura may either be due to complex macroglobulin or hyperviscosity secreted by tumor cells that interfere with clotting factors and platelet function.

CONCLUSIONS:

Purpura, lymphadenopathy spurious and blood cell counts can occur individually due to varied reasons, and in combination is indicative of paraprotein secreting tumors. Clinical and laboratory evaluation of spurious leukocytosis are essential for proper diagnosis and timely treatment.

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