Case Report

Reactive Lymphocytosis: A Diagnostic Dilemma in Pleural Effusion

Uma[1], Shelly Sehgal[2]*

[1]Department of Pathology, Veer Sawarkar Arogya Sansthan, Karawal Nagar, Delhi, India
[2]Department of Pathology, Swami Dayanand Hospital, Dilshad Garden, Delhi, India

Keywords: *Effusion;Immunophenotyping; Lymphoma*

ABSTRACT

Effusions containing numerous lymphocytes may be due to inflammatory processes, to non-specific reactions complicating other diseases or tolymphoid malignancies. In many cases it is difficult to make a differential diagnosis on morphological criteria alone. We present a case of 25 year old male who presented with cough and fever for one month along with left sided pleural effusion. Pleural fluid differential count showedlymphocytosis. Cytology smears showed the presence of large mononuclear cells with high N:C ratio,convoluted nucleus and prominent nucleolus. On immunophenotyping it was proved to be a case of reactive T lymphocytosis. A single lymph node was also found in upper cervical region which showed epithelioid cell granulomas with ZN stain for AFB positive. To concludereactive lymphocytes are difficult to distinguish from lymphoma onmorphology alone. Diagnostic accuracy can be increased by history, clinical examination and the use of ancillary techniques like immunophenotyping or immunocytochemistry.

***Corresponding author:**
Dr. Shelly Sehgal, Specialist Pathologist, Department of Pathology, Swami Dayanand Hospital, Dilshad Garden, New Delhi- 110092
Phone: +91 9711196106
E-mail: shellysehg@gmail.com

Introduction

Pleural effusions, the result of the accumulation of fluid in the pleural space, are a common medical problem. They can be caused by several mechanisms including increased permeability of the pleural membrane, increased pulmonary capillary pressure, decreased negative intrapleural pressure, decreased oncotic pressure, and obstructed lymphatic flow[1]. The cytological diagnosis of serous effusions containing numerous lymphoid cells may present difficulty in differentiating a reactive from a malignant process .

Here, we present an interesting case of pleural effusion with lymphocytosis which posed a diagnostic problem.

Case Report

25 years old male, presented with sudden onset dyspnea and fever with non -productive cough for one month.On examination there were extensive decreased breath sounds on left side with stony dullness. Chest radiographshowed leftsided massivepleural effusion (fig.1). Pleural tap was done which revealed 400ml of straw coloured fluid and sent to cytopathology laboratory for evaluation.

On examination cytospin smears showed highcellularity with predominance of large mononuclear cells with high N:C ratio,nuclear convolusions and 0-2 prominent nucleolus(fig. 2)**.** Few scattered neutrophils, macrophages and occasional plasma also noted.Since by morphology no conclusive opinion could be made.

Flow cytometry was performed which showed 95% of the total acquired events had bright Cd45 expression and a low side scatter. Some of these cells (18%) of the total acquired events showed slightly less brighter CD45 expression [mature lymphocytes]. 83% of the total gated cells show positivity for T-celllineage like CD7,CD2,CD3, and CD5 (fig3).The brightest CD45 positive population [reactive lymphocytes] showed 64%CD8 and 30%CD4 (fig. 4).Only 11% of the mature lymphocytes were B-lymphocytes(CD19 positive) with no light chain restriction positive.(fig.5). These cells were negative for common acute lymphoblastic leukemia antigen CD10 and CD34 which is a stem cell marker**.**These immunophenotyping findings suggested reactive T cell proliferation.Also, on further evaluating the patient we found a tiny cervical lymph node. FNA from this showed epithelioid cell granulomas in alymphoid background and ZN stain showed acid fast bacilli.

So, diagnosis of tuberculous effusion was given and anti-tubercular treatment was started. There was a rapid clinical response including resolution of fever and pleural effusion.

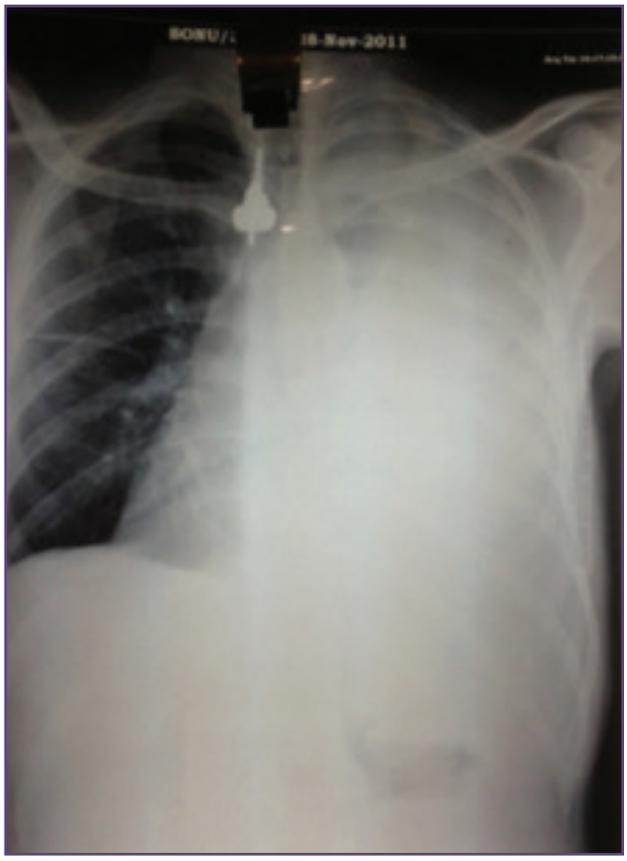

Fig. 1: Chest radiograph showing left sided massive effusion.

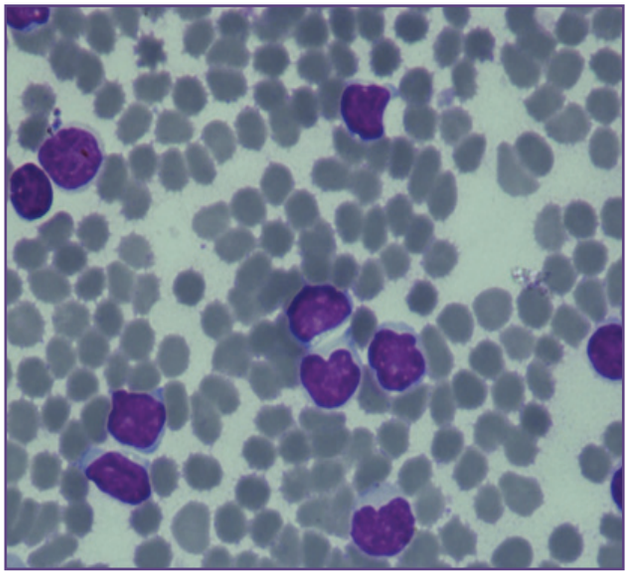

Fig. 2: Photomicrograph showing pleural fluid lymphocytosis. Cells have high N:C ratio with convoluted nuclei and prominent nucleoli.(Giemsa, 40X)

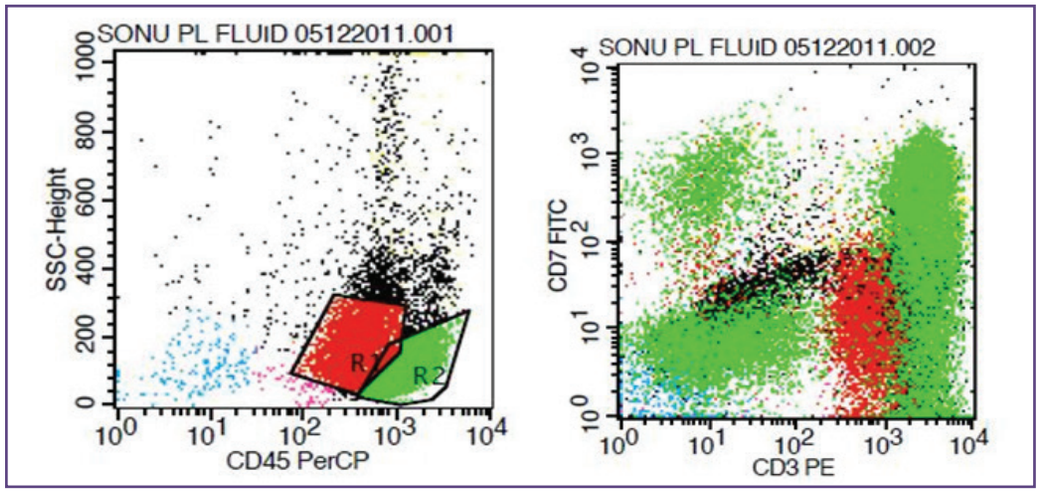

Fig. 3: Flow cytometry dot plots showing bright Cd45 expression and a low side scatter in 95% of the total gated cells. 83% of these cells show positivity for T-celllineage like CD7 and CD3.

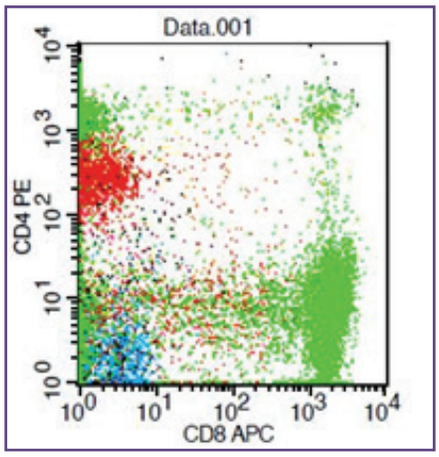

Fig. 4: Flow cytometry dot plots showing 64% CD8 and 30% CD4 lymphocytes.

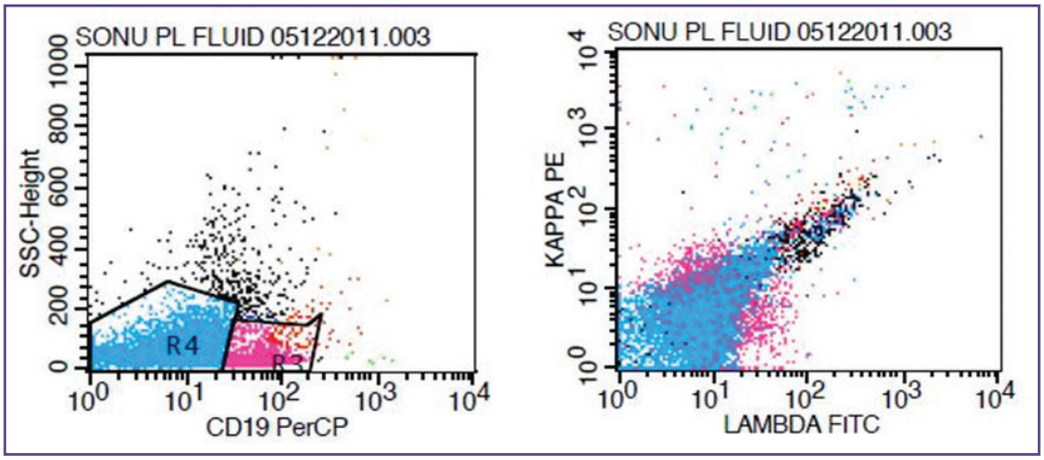

Fig. 5: Flow cytometry dot plots showing 11% B-lymphocyteswith no light chain restriction.

Discussion

Tuberculous pleuritis is a common manifestation of extrapulmonary tuberculosis (TB) and is the most common cause of pleural effusion in many countries.[2] Pleural TB occurs as a result of a TB antigen entering the pleural space, usually through the rupture of subpleural focus, followed by a local, delayed hypersensitivity reaction mediated by CD4+ cells.[3] This process may occur during primary or reactivation TB and may or may not involve viable bacilli entering the pleural space.[4]

The presence of mycobacterial antigens in the pleural space elicits an intense immune response, initially by neutrophils and macrophages [5,6], followed by interferon (IFN)-c-producing T-helper cell (Th) type 1 lymphocytes [3, 7], resulting in a lymphocyte-predominant exudative effusion. This cellular trafficking is facilitated by homing surface markers and chemokine gradients. [8,9] This intense but poorly understood local immune response by sensitised lymphocytes to TB antigen is synonymous with the Koch phenomenon. [10]

Pleural fluid lymphocytosis is non-specific and may be found in malignancy, tuberculosis, collagen vascular diseases, sarcoidosis and lymphoma. [11]

It is agreed that serous cavity involvement by alow grade lymphoma is notoriously difficult to differentiate from a reactive process on the basis of cytomorphology alone. [12]

In our case also the cytomorphology alone was inconclusive.Therefore, we applied flow cytometry to come to conclusion. On immunophenotyping, it was proved to be a case of reactive T lymphocytosis. Also a thorough search for any peripheral lymph nodes revealed a single lymph node in upper cervical region.FNA from same showed epithelioid cell granulomas in alymphoid background. ZN stain for AFB was also positive.

Immunophenotyping by flow cytometric analysis of body cavity fluids can be a very useful adjunct to conventional diagnostic cytopathology in the evaluation of serous effusions for lymphomatous involvement. [13]

In a study of Czader and Ali, immunophenotyping by flow cytometry modified the provisional cytopathologic diagnosis in 16% of 115 consecutive serous cavity effusions and this included 10 benign and atypical or suspicious cases that became malignant. [14]

Satouchi et al. could establish definite diagnosis of lymphoma in 2 cases, only by flow cytometric examination of pleural effusion. [15]

Cytomorphology and immunophenotyping in combination can improve the diagnostic accuracy. Bangerter et al. in a study of 33 lymphomatous and 21 reactive effusions found 7 false-negative cases, if only one method was used but the combined strategy of cytomorphology and immunophenotyping had 100% sensitivity and 100% specificity. [16]

Conclusion

To conclude reactive lymphocytes are difficult to distinguish from lymphoma on morphology alone. Diagnostic accuracy can be increased by meticulous clinical examination and the use of ancillarytechniques.

Acknowledgement

None

Funding

None

Conflict of interest

No

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