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Case Report

Lymphoma presenting as the first finding in pleural fluid cytology: A rare cytologic presentation

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ABSTRACT

Malignant hemato-lymphoid neoplasms presenting as the initial finding in pleural effusion cytology is one of the rare challenges a pathologist may encounter in practice among lymphocyte-rich effusions. Meanwhile, effusion cytology is an easily available, inexpensive diagnostic tool in our setting. Cytomorphological features provide crucial insights into the nature of the disease, which along with immunocytochemistry may help in solidifying the diagnosis. Here we present a rare case of a 17-year-old patient, who initially presented with pleural effusion that turned out to be lymphoma on cytological examination. Cell blocks were prepared and immunocytochemistry was performed for CD5 and CD23. Tumor cells showed positivity for both CD5 and CD23, confirming the diagnosis of small lymphocytic lymphoma.

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1. Introduction

Infiltration of the lining of serous cavities in the body results in effusion which can be due to either benign or malignant causes.[1,2] Among malignant pleural effusions, ascites lymphoma accounts for 10.0-15.0% followed by lung, breast, and ovary carcinoma.[1] Patients with pleural effusions present with respiratory distress and require immediate therapeutic intervention.[2–4]

Pleural fluid analysis along with cytological examination is the readily available and cost-effective method of investigation for unilateral pleural effusions.[3,4] Differentiating malignant effusion due to lymphoma from lymphocyte-rich effusion poses a diagnostic challenge to pathologists due to its similar cytomorphology.[2–5] The estimated sensitivity for detecting malignancy from fluid cytology ranges from 40.0% to 87.0%.[3] Cytopathological findings of effusions are confirmed with immunocytochemistry and flowcytometry.[6]

2. Case Report

A 17-year-old male patient, a non-smoker presented to the hospital with complaints of dyspnea, dry cough, and right-sided chest pain, which had worsened in the past 20 days along with anorexia, loss of weight & apetite and low-grade fever for the past 7 months. There was no history of asthma or occupational exposure. On physical examination patient was dyspneic with a respiratory rate of 24/ minute and SPO_2 was 90%. On further examination, few discrete cervical lymph nodes were identified. Chest X-ray revealed right-sided pleural effusion. Montoux test was negative.

A pleural tap was performed and 20 ml was aspirated which was grossly straw coloured with a tinge of blood. Fluid was sent for analysis and cytopathological examination. Routine and cytospin smears were prepared

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followed by Haematoxylin and Eosin and Papanicolaou staining and examined under the light microscope. The smears were highly cellular with a predominant population of dyscohesive small to medium-sized lymphoid cells with minimal cytological atypia (Figures 1 and 2).

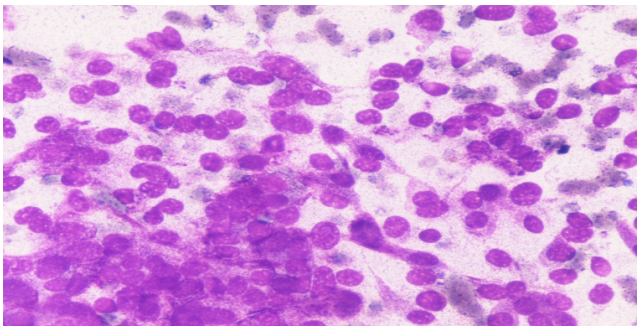

Figure 1: Smears were highly cellular with a predominant population ofdyscohesive small to medium-sized lymphoid cells with minimal cytological atypia and fine granular chromatin with minimal cytoplasm. Haematoxylin and Eosin x 40X.

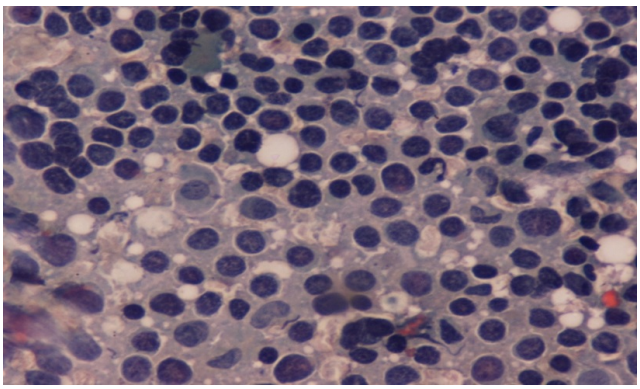

Figure 2: Smears were highly cellular with a predominant population ofdyscohesive medium-sized lymphoid cells with fine granular chromatin and minimal cytoplasm. Papanicolaou x 40X.

Positron Emission Tomography and Computed Tomography scan revealed metabolically active cervical lymph nodes. Cell blocks were prepared and immunocytochemistry was performed for CD5, CD23, SOX11, Cyclin D1. Tumor cells showed positivity for both CD5(Figure 3) & CD23(Figure 4) and negative for SOX11 & Cyclin D1. Flow cytometry of the fluid showed positivity for CD5, CD20, CD23, and kappa confirming the diagnosis of small lymphocytic lymphoma/ chronic lymphocytic leukemia.

The patient was treated with a chemotherapy regimen of Fludarabine-125mg/m^2, Cyclophosphamide-1000mg/m^2 and Rituximab-375mg/m^2 for 6 cycles. The patient was followed up with a Positron Emission Tomography and Computed Tomography scan after 3 weeks that showed a complete metabolic response. Now the patient is asymptomatic and under close follow-up.

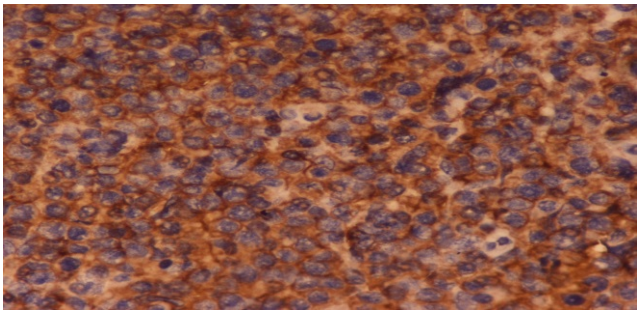

Figure 3: Immunocytochemistry showed membranous positivity for CD5 in tumor cells. IHC CD 5x 40X.

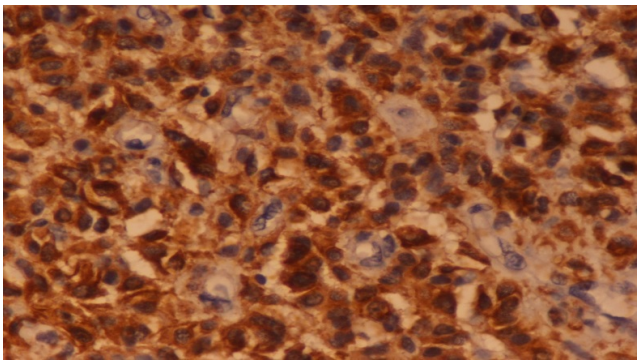

Figure 4: Immunocytochemistry showed membranous positivity for CD 23 in tumor cells. IHC CD 23x 40X.

3. Discussion

Pleural effusion may be due to benign or malignant conditions. Malignant effusions are a common problem in the treatment of patients with lung cancer, breast cancer, and lymphoma. [1,2] Benign conditions may be due to infectious causes or as a result of some systemic diseases that present as lymphocyte-rich effusions. [1,7–9]The benign effusion occurs mostly due to infectious etiology, including tuberculosis, viral and fungal infections. Whereas, malignant causes may be due to non-hematolymphoid or hemato-lymphoid causes. Non-hemato-lymphoid causes include lobular breast carcinoma, small cell carcinoma of the lung, gastric signet ring cell carcinoma, and malignant melanoma. The hemato-lymphoid causes include lymphomas. [1–5]

When the possibility of non-hemato-lymphoid causes is ruled out, assessment in the direction of hemato-lymphoid malignancy is carried out based on the cell size as small/ medium or large cell lymphomas. Small or medium cells have diameters less than 2 mature lymphocytes or RBCs, whereas large cells have diameters exceeding 3 or 4 times of lymphocytes or RBCs. [1]

A schematic representation of the approach to hemato-lymphoid malignancies is shown in Figure 5. Cytomorphological similarities between reactive and neoplastic small/medium-sized cell predominant fluids pose a diagnostic challenge to pathologists.[1–3] Reactive effusion is composed of polymorphic cells predominantly T lymphocytes which lack nuclear atypia. Meanwhile, the latter entity shows highly cellular smears composed of monomorphic cells with marked cellular atypia/ pleomorphism. Frequent mitoses and apoptosis can also be seen. Large-sized cell predominant effusion is composed of large cells with significant nuclear atypia in a background of necrosis and apoptosis.[2,4,7]

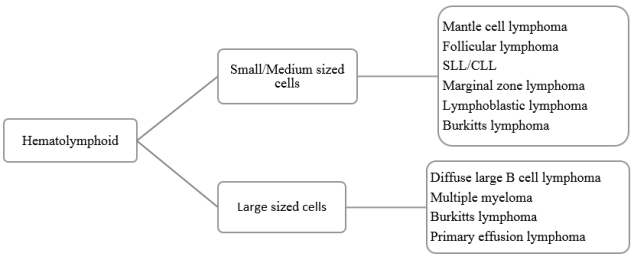

Figure 5: Showing categorization of hemato-lymphoid malignancies

Although cytological morphology aids the diagnosis of hematological malignancies, ancillary tests like immunocytochemistry, flow cytometry or molecular methods are essential to confirm the diagnosis. In patients with Small lymphocytic lymphoma/Chronic lymphocytic leukemia, cells show positivity for CD5 and CD23.[6,9–11]

In 2023, Thouil et al reported a case of 55 years old man who presented with right-sided pleural effusion, immunophenotyping of which showed B cell population with CD19+, CD23+, CD43+. The diagnosis of CLL was made and was treated with Fludarabine, Cyclophosphamide, and Rituximab therapy.[12] Sharma et al in 2022 reported a case of right pleural effusion in a 66-year-old female. Fluid cytology revealed malignant cells that showed CD19+, CD5+ and CD23+.[13] A case of CLL/SLL in a 79-year-old male patient was reported by Emad et al in 2017 and the patient was treated with Obinutuzumab.[14]

4. Conclusions

This article might be an eye-opener for pathologists to differentiate malignant neoplasms from benign entities. The horizons of cytopathology together with ancillary tests such as Immunocytochemistry or Flow cytometry has proven more useful in making prompt diagnosis by minimally invasive techniques like thoracocentesis.

5. Source of Funding

None.

6. Conflict of Interest

None.

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