Quiz Case

Effusion cytology and hematopoietic process

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An 18-year-old male presented with intermittent chest pain along with dyspnea and cough for 1 month. On examination, the patient had massive pleural effusion (PE) on the right side. His contrast-enhanced computed tomography suggested a large mildly enhancing anterior mediastinal mass with the right-sided PE [Figure 1a]. His complete blood count (CBC) findings were within normal limits. One liter of hemorrhagic fluid was received and pleural fluid smears were prepared from centrifuged deposits and examined [Figure 1b-d].

Figure 1: (a) Contrast-enhanced computed tomography showing a large mildly enhancing anterior mediastinal mass (depicted by arrow) with the right-sided pleural effusion, (b) two distinct population of cells appreciated consisting of small- and medium-sized cells (Papanicolaou ×10), (c) higher power shows tumor cells with high N: C ratio, convoluted and lobulated nuclei with scant cytoplasm resembling blasts (Papanicolaou ×40), (d) Giemsa stained smear showing the presence of tumor cells with convoluted, lobulated nuclei with scant cytoplasm (Giemsa ×40).

QUESTION

Q1. What is your interpretation?
   a. Metastasis from Hodgkin lymphoma
   b. Metastasis from non-Hodgkin lymphoma
   c. Leukemic infiltrate
   d. Metastasis from germinoma/semionoma
   e. Metastasis from thymic carcinoma.

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ANSWER

Q1:

b. Metastasis from non-Hodgkin lymphoma

A1: In Hodgkin’s lymphoma, there is a polymorphic background of cells consisting of lymphocytes, eosinophils, plasma cells, and histiocytes. The characteristic “Reed Sternberg cell” is present, which possesses a large lobulated nucleus. The cells may be symmetrically paired (mirror shaped), complex, or multiple. They have large eosinophilic nucleoli and abundant pale fragile cytoplasm. These features were lacking in cytocentrifuged cell deposits, thus ruling out metastasis from Hodgkin lymphoma (HL).

Patients with T-cell leukemia may present with an anterior mediastinal mass and PE. However, since the CBC and peripheral blood smear findings were within normal limits, a leukemic infiltrate can be ruled out.

Germ cell tumors (GCTs) account for 6–18% of mediastinal masses. About 20% of mediastinal GCTs are malignant and include seminomas and non-seminomatous tumors such as teratocarcinoma, yolk sac tumor, embryonal carcinoma, choriocarcinoma, and mixed types. Primary germinomas virtually only occur in young males.

Based on cytomorphology, we can rule out non-seminomatous GCT. In seminoma, the cells are fragile and have a tigroid background. They have vesicular nuclei with prominent nucleoli. Dispersed lymphocytes accompanying tumor cells are also present. However, due to the absence of tigroid background in centrifuged deposits, the diagnosis is more in favor of non-HL. An immunohistochemistry (IHC) is, however, desirable for a confirmatory diagnosis.

Thymic carcinoma metastasis can be safely ruled out based on cytomorphology, as these cells are loosely cohesive with large tumor cells with abundant opaque eosinophilic cytoplasm and the presence of prominent nucleoli in a necrotic background.

In non-HL, we get a monomorphic population of cells with variation in cell size and nuclear features. Small cells are <1.5 times the size of normal lymphocyte. Medium-sized cells are 1.5–2 times while larger cells are 2–3 times the size of normal lymphocyte. In this case, we could appreciate both small- and medium-sized cells. Few of the medium-sized cells showed high N:C ratio and convoluted, lobulated nuclei with scant and fragile cytoplasm resembling blasts. Anisonucleosis could be appreciated with dense chromatin and inconspicuous nucleoli. Few of the cells showed the presence of scant, fragile cytoplasm. These cytomorphological features are favoring metastasis from non-HL, possibly lymphoblastic lymphoma, T-cell type, but it needs to be proved by IHC.

FURTHER INVESTIGATIONS AND FOLLOW-UP

A cell block was made [Figure 2a], followed by immunohistochemical evaluation utilizing a panel consisting of leukocyte common antigen (LCA), CK, terminal deoxynucleotidyl transferase (TdT), CD3, CD5, CD10, CD19, CD20, CD30, Bcl2, Bcl6, kappa, lambda, CD117, PLAP, and Ki 67. The cells were positive for LCA, Tdt, CD3, CD5, and Ki 67 [Figure 2b-f] while the rest of the markers were negative, thus confirming our cytomorphological diagnosis of lymphoblastic lymphoma, T-cell type, which was later confirmed on histopathology.

Q2. PE occurs in lymphoma because

a. Impaired lymphatic obstruction
b. Pleural infiltration by the tumor
c. Venous obstruction
d. All the above.

Q3. Most common reason for PE in lymphoma is

a. Impaired lymphatic obstruction
b. Pleural infiltration by the tumor
c. Venous obstruction
d. Pulmonary infection.

Q4. The criteria for number of blasts that should be present in bone marrow to differentiate between T-lymphoblastic lymphoma from T-lymphocytic leukemia are

a. >10% blasts in marrow
b. >20% blasts in marrow
c. >25% blasts in marrow
d. >30% blasts in marrow.

ANSWERS TO ADDITIONAL QUIZ QUESTIONS

Q2: d, Q3: a, Q4: c.

A2: PE in lymphoma can emerge from the results of the variety of mechanisms, such as impaired lymphatic drainage due to mediastinal lymph nodes or thoracic duct obstruction, pleural or pulmonary infiltration by tumor, venous obstruction, pulmonary infection, or radiation therapy.

A3: Lymphatic obstruction is the most frequent factor for PE.

A4: The distinction between T-lymphoblastic lymphoma from T-lymphocytic leukemia is based on the degree of bone marrow involvement such that patients with ≥25% marrow blasts are designated as having leukemia.

BRIEF REVIEW OF THE TOPIC

Lymphoma accounts for approximately 13% of all childhood cancers and is the most common cause of a mediastinal mass in children. Sixty percent of all lymphomas in this age group are non-HLs while the remaining 40% are HL. Roughly, two-third of Hodgkin’s lymphoma and 50% of
non-Hodgkin's lymphoma present with anterior mediastinal mass. However, only 5% of Hodgkin's lymphomas present with PE and deposit as compared to lymphoblastic lymphoma (non-Hodgkin's lymphoma) which causes PE and deposits in 50–75% of the cases.\(^3\),\(^6\)

T-LBL is a rare type of non-Hodgkin's lymphoma, with an overall incidence of ~0.1/100, 1000 inhabitants/y, and predominantly occurs in male adolescents or young adults.\(^7\) T-cell lymphoblastic lymphoma (T-LBL) constitutes approximately 85–90% of all LBL and presents mainly with rapidly enlarging masses in the mediastinum, cervical lymphadenopathy, and body cavity effusions. T-LBL arises from precursor T-lymphocytes and is well known for its low incidence, poor prognosis, and short survival time, as patients are usually diagnosed with advanced-stage disease.\(^8\) Jin et al. reported that 45.7% of cases of T-LBL presented with bulky mediastinal masses and 62.9% of cases presented with pleural and/or pericardial effusions, and patients are usually diagnosed with advanced-stage cancer.\(^8\)

With intensive chemotherapy treatment, the complete remission rate can be very high and many patients can be cured. Thus, an early diagnosis by fluid cytology and immunocytochemistry can help in earlier treatment of patients.

Furthermore, flow cytometry has been used by cytopathologists in various parts of the world for diagnosing various hematolymphoid malignancies in body fluids. It is a rapid, reproducible, sensitive, and quantitative method for immunophenotyping of cells, which utilizes a panel of fluorescent dye-tagged antibodies directed mostly against the cell surface markers. The combination of cytology and FC also enables an accurate and rapid diagnosis of T-LBL on FNA and effusion cytology specimens.\(^9\)

**SUMMARY**

Effusion cytology is an easily accessible, inexpensive diagnostic tool in the diagnosis of malignancies. They may often be the first manifestation or may occur during the disease course. Its cytomorphological features when combined with immunocytochemistry can provide a fairly accurate diagnosis and an early breakthrough in patient management. The presence of tumor cells in effusion is not only associated with poor patient outcome but is also a predictor of disease relapse after chemotherapy and decreased survival.

**COMPETING INTEREST STATEMENT BY ALL AUTHORS**

The authors declare that they have no competing interest.

**AUTHORSHIP STATEMENT BY ALL AUTHORS**

Each author has participated sufficiently in the work and takes public responsibility for appropriate portions of the content of this article. All authors read and approved the final manuscript. Each author acknowledges that this final version was read and approved.

**ETHICS STATEMENT BY ALL AUTHORS**

As this is the case without identifiers, our institution does not require approval from the Institutional Review Board (IRB) (or its equivalent).
LIST OF ABBREVIATIONS (In alphabetic order)

GCT – Germ cell tumor
HL – Hodgkin’s lymphoma
NHL – Non-Hodgkin's lymphoma
T-LBL – T-Lymphoblastic lymphoma.

EDITORIAL/PEER-REVIEW STATEMENT

To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a double-blind model (authors are blinded for reviewers and vice versa) through automatic online system.

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