Quiz Case

Plasmacytoid cells in a thyroid aspirate – Look before you leap

Mona Agnihotri, MD1, Leena Naik, MD1, Kanchan Kothari, MD1, Jaya Kharat, MD1

1Department of Pathology, Seth G.S. Medical College and K.E.M. Hospital, Mumbai, Maharashtra, India.

CASE HISTORY

A 60-year-old female with hypothyroidism under treatment presented with neck swelling for 2 months. Ultrasonography showed bulky right thyroid lobe (6.4 × 4.2 × 3.1 cm) with multiple heterogeneous nodules and microcalcification and with multiple necrotic cervical lymph nodes. Fine-needle aspiration (FNA) of the largest thyroid nodule (3 × 3 × 2 cm) is shown in Figure 1.

Figure 1: (a) Right thyroid FNA. Cellular smear showing predominantly discohesive plasmacytoid cells of variable sizes (Giemsa stain, ×400). (b) Few binucleate and multinucleate cells present. Background shows a few scattered lymphoglandular bodies (Giemsa stain, ×600). (c) Cells have eccentric nuclei with finely stippled chromatin and moderate amount of cytoplasm (Papanicolaou stain, ×400). (d) Discohesive plasmacytoid cells. (Giemsa stain, ×1000).

What is your interpretation?

a. Hurthle cell neoplasm
b. Non-Hodgkin's lymphoma
c. Medullary carcinoma
d. Metastatic carcinoma

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Answer
The correct answer is b. Non-Hodgkin's lymphoma.

Figure 2: Cells expressing LCA immunoreactivity (ICC, ×400).

Thyroid FNA smears were highly cellular, showing predominantly discohesive plasmacytoid cells of variable sizes [Figure 1a]. Also seen were binucleate and multinucleate cells [Figure 1b]. The cells had eccentric nuclei with finely stippled chromatin and moderate amount of cytoplasm [Figure 1c]. Lymph node aspirate also showed similar cytomorphological features. The location, that is, mass in the thyroid, along with the above cytologic features led to a high suspicion of diagnosis of medullary thyroid carcinoma (MTC, plasmacytoid type) with lymph node metastasis. Serum calcitonin was advised. The calcitonin level was found to be less than 2 pg/ml. On review of the slides, it was observed that the background had scattered lymphoglandular bodies (LGBs). One Pap stained slide was then destained for immunocytochemistry (ICC) and the cells showed strong immunoreactivity for leukocyte common antigen (LCA) (CD45) [Figure 2]. The possibility of non-Hodgkin lymphoma (NHL) with plasmacytic differentiation was highly considered. In the meanwhile, a lymph node biopsy was also done for further workup. The cells showed immunoreactivity for LCA, cluster designation (CD)79a, CD10, BCL2, and EMA and non-immunoreactivity for calcitonin, CD138, CD56, CD3, CD20, CD30, CD23, and anaplastic lymphoma kinase (ALK1). The proliferative index (MIB1) was 40%. The final diagnosis of high-grade non-Hodgkin B-cell lymphoma with plasmacytic differentiation was rendered.

ADDITIONAL QUIZ QUESTIONS

Q1. Which immunochemistry panel will best help in the diagnosis?
   a. Calcitonin, synaptophysin, chromogranin
   b. Calcitonin, LCA, CD138
   c. LCA, synaptophysin, CK
   d. Thyroglobulin, chromogranin, calcitonin.

Q2. All the following are features of medullary thyroid carcinoma except
   a. Dispersed tumor cells
   b. Eccentric nuclei
   c. Stippled chromatin
   d. Blue cytoplasmic granules on MGG.

Q3. Lymphoglandular bodies are derived from:
   a. Nuclear remnants
   b. Stain precipitation
   c. Cytoplasmic fragments
   d. Immunoglobulin.

Answers of additional Quiz Questions
Q1.b; Q2.d; Q3.c.

BRIEF REPORT
Clinically, a mass in the thyroid and the presence of discohesive plasmacytoid cells in a background containing amyloid/amyloid-like material on cytology smears leads to a diagnosis MTC as it is the most common carcinoma associated with the above two features among thyroid malignancies.[1] These features can, however, also be seen in other rare thyroid neoplasms such as plasma cell neoplasm and NHLs with plasma cell differentiation.[2] It is important to look for other supporting cytomorphological features that are often reported in MTC, like red cytoplasmic granules (88%), neuroendocrine type salt and pepper or stippled nuclear chromatin (65%), binucleated and multinucleated cells (70%), cytoplasmic “triangular” tails (58%), and amyloid.[3] Amyloid should be confirmed by Congo-red stain and serum calcitonin levels must be advised.

The presence of LGBs, cartwheel chromatin pattern, and Dutcher bodies can indicate malignant lymphoma and plasmacytoma.[4] The monomorphic appearance, granular cytoplasm, intranuclear inclusions, and eccentric nucleus of MTC cells can mimic Hürthle cell neoplasm and Hürthle cell variant of papillary thyroid carcinoma (PTC).[5] The finely textured chromatin, prominent macronucleoli, and blue cytoplasmic granules on Romanowsky stains correctly identify Hürthle cell neoplasm.[5] The presence of characteristic nuclear features of PTC, dense cytoplasm, and positive immunoreactivity for thyroglobulin distinguishes it from MTC. Rarely metastatic tumor, particularly melanoma warrants consideration but the presence of pigment and macronucleoli helps in the diagnosis. Serum calcitonin and immunochemistry for calcitonin, thyroglobulin, LCA, CD 138, and HMB 45 are of great help for confirmation and in avoiding the diagnostic dilemmas.
SUMMARY
The diagnosis of lymphomas with plasmacytic morphology in the thyroid can be overlooked and misinterpreted as MTC due to rarity and overlapping cytomorphologic features. Clinical correlation, precise study of the cytological features, and carefully screening the thyroid smears for LGBs in the background are crucial to avoid misdiagnosis, before instituting a definitive therapy.

COMPETING INTEREST STATEMENT BY ALL AUTHORS
The authors declare that they have no competing interest.

AUTHORSHIP STATEMENT BY ALL AUTHORS
MA carried out cytological evaluation and reference work and drafted the manuscript. LN carried out the cytological evaluation and clinico-pathological co-relation. KK conceived the study, edited the manuscript and formatted the questions. JK helped to draft the manuscript and perform ICC. All authors read and approved the final manuscript.

ETHICS STATEMENT BY ALL AUTHORS
This study was conducted with approval.

LIST OF ABBREVIATIONS (In alphabetic order)
ALK-Anaplastic lymphoma kinase
FNA-Fine-needle aspiration
ICC-Immunocytochemistry
LCA-Leukocyte common antigen
LGB-Lymphoglandular bodies
MTC-Medullary thyroid carcinoma
NHL-non-Hodgkin lymphomas
PTC- Papillary thyroid carcinoma.

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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How to cite this article: Agnihotri M, Naik L, Kothari K, Kharat J. Plasmacytoid cells in a thyroid aspirate – Look before you leap. CytoJournal 2022;19:13.

HTML of this article is available FREE at: https://dx.doi.org/10.25259/Cytojournal_23_2020