

# Response to comment on "A stepwise approach to fine needle aspiration cytology of lymph nodes"

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To the Editor,

We read Caputo et al.'s letter [1] regarding our recently published review, "A Stepwise Approach to Fine Needle Aspiration Cytology of Lymph Nodes," with great interest and we really appreciate to their keen observation and critique to our review [2]. Their critique of our publication focuses on three primary issues: (1) The Sydney system's strong recommendation for reporting the nosologic entity's nature (lymphoid/metastatic) [3]. (2) Our proposed stepwise system's exclusive focus on morphology, overlooking ancillary techniques like flow cytometry and polymerase chain reaction. (3) The heightened risk of malignancy in the AUS-ALUS (atypical, undermined significance–atypical lymphoid uncertain significance) category, as highlighted in Gupta et al.'s study [4], attributed mainly to the non-use of ancillary techniques.

While we align with the Sydney system's recommendation to identify the nosologic entity and integrate ancillary tests in the diagnostic process, our approach in the review was broader. In Fig. 10's diagnostic algorithm, we referenced "sufficient features for malignancy," intending to encompass all feasible test findings, including morphology, immunocytology, and molecular tests. This was not explicitly stated, but it was implied [2].

Our focus initially was on the morphological features of lymph node fine needle aspiration cytology (FNAC), acknowledging that ancillary tests are not always accessible. In Korea, for in-

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Department of Hospital Pathology, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 271 Cheonbo-ro, Uijeongbu 11765, Korea Tel: +82-32-820-3160, Fax: +82-32-820-3877, E-mail: ychong@catholic.ac.kr stance, excisional biopsy on lymph nodes post-FNAC is common, with most ancillary testing conducted on histologic sections. This preference stems from the rapid and cost-effective nature of excisional biopsies specifically in Korean medical environment. Korean clinicians and patients often opt for confirmatory diagnoses involving more comprehensive sample analyses.

Rapid advancements in molecular pathology have undoubtedly enhanced lymphoma understanding and treatment. However, many countries still struggle to fully incorporate these tests in cytodiagnostics and it sometimes causes subsequent confusion during the diagnostic process in the clinical practice. The study by Gupta et al. [4], also applying the Sydney system, reflects this limitation in India, as ancillary techniques were scarcely employed. Recent detailed molecular research on lymphoid neoplasms has divided the academic community, resulting in the development of two distinct classification systems on histologic diagnosis: the 5th edition of the World Health Organization classification (WHO-HAEM5) and the International Consensus Classification (ICC), which brings many confusions to the practicing pathologists in the daily practice [5]. On the other hand, the Sydney system for cytologic diagnosis, in our view, is versatile, accommodating both contexts where molecular pathology is feasible and scenarios reliant solely on morphological evaluation [3,6].

We concur with Caputo et al.'s observations [1] and aimed our review to enrich the diagnostic process, focusing on morphological details. Our comprehensive algorithm, incorporating various morphological features, seeks to streamline and improve diagnostic accuracy. In scenarios where specimen quantity limits further testing, or when additional molecular tests are impractical due to cost, infrastructure, or even sociocultural constraints, our approach offers direct support to cytopathologists. Hopefully, further validation studies on the Sydney System using real cases of lymph node FNAC in Korea or Asian population should be followed for the reconfirmation of the clinical efficacy as proven in previous studies [4,6]. Looking forward, we anticipate that advancements in digital cytopathology and artificial intelligence image analysis will enhance cancer diagnosis, subtype differentiation, and molecular mutation prediction in near future, as Caputo et al. also suggested [7-9].

# **Ethics Statement**

Not applicable.

## Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

#### **Code Availability**

Not applicable.

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Conceptualization: YC, GP, HJC, HJK, CSK, SSL. Supervision: GP, SSL. Visualization: YC. Writing—original draft: YC. Writing—review & editing: YC, GP, HJC, HJK, CSK, SSL. Approval of final manuscript: all authors.

## **Conflicts of Interest**

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