Broncho-alveolar Lavage Cytology Evidence of Pulmonary Metastasis by Neuroblastoma

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Introduction

Neuroblastoma (NB) is the most frequent pediatric extracranial solid tumor. It exhibits a high metastatic rate, with approximately 70% of patients presenting with metastasis at diagnosis. While bone and liver are the most common sites, lung involvement occurs in 1.3 to 6.6% of cases.[1,2] To our knowledge, this report describes the first instance of NB pulmonary metastasis diagnosed using broncho-alveolar lavage (BAL) samples.

Case History

A 1-year-old female pediatric patient previously diagnosed with abdominal *MYC-N*-amplified NB presented 8 months later with dyspnea and fever. Chest scan by computed tomography revealed multiple bilateral parenchymal thickenings, suggestive of infection. A BAL was performed. The recovered fluid was processed using the cell-block (CB) method, involving formalin fixation, centrifugation, agar pre-embedding, and paraffin embedding.[3] Three-micron sections were stained with hematoxylin and eosin.

Microscopic examination revealed a highly cellular specimen composed predominantly of macrophages. However, rare smaller cells with a high nuclear/cytoplasmic ratio, hyperchromatic nuclei, occasional prominent nucleoli, cell–cell adhesion, and instances of cell "cannibalism" were also observed. Immunocytochemistry revealed these cells to be CD56+, Tyrosine-hydroxylase+, and Synaptophysin+ (►**Figs. 1** and **2**). Based on these findings, a diagnosis of pulmonary metastasis from NB was made.

Discussion

The peculiarity of this case lies in diagnosing NB pulmonary metastasis via a minimally invasive BAL procedure. BAL, introduced in 1974, allows the collection of cells and secretions from the distal airways, providing valuable diagnostic information.[4]

The patient's prior NB diagnosis included *MYC-N* amplification, a marker of poor prognosis. Microscopically, *MYC-N*-amplified NBs often show enlarged and prominent nucleoli (►**Fig. 3**).[5] The BAL sample maintained these microscopic features.

We also noted cell "cannibalism," a survival mechanism activated under stress, where neoplastic cells engulf others.[6] While not specific to NB, its presence raised suspicion. Since only a few cells displayed these features amidst numerous macrophages, immunohistochemistry via the CB technique was essential for confirmation. This is particularly important in cases with limited cellularity, where traditional histologic

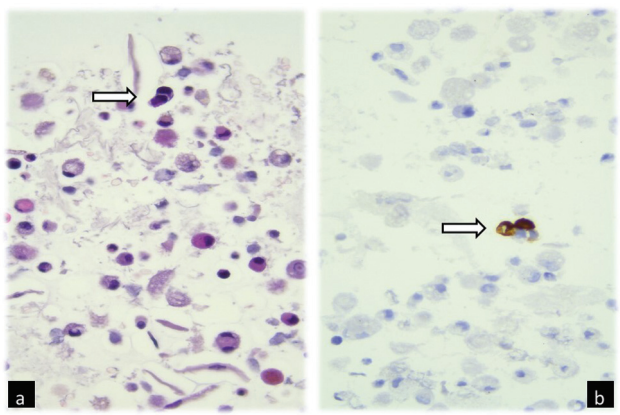

Fig. 1 Broncho-alveolar lavage cell-block photomicrograph showing (**a**) two neoplastic cells with altered nuclear–cytoplasmic ratio and nuclear hyperchromasia (arrow) among macrophages and exfoliation cells (H-E, 400×); (**b**) neoplastic cells (arrow) positive for tyrosine-hydroxylase immunohistochemistry, characteristic of neuroblastoma (400×).

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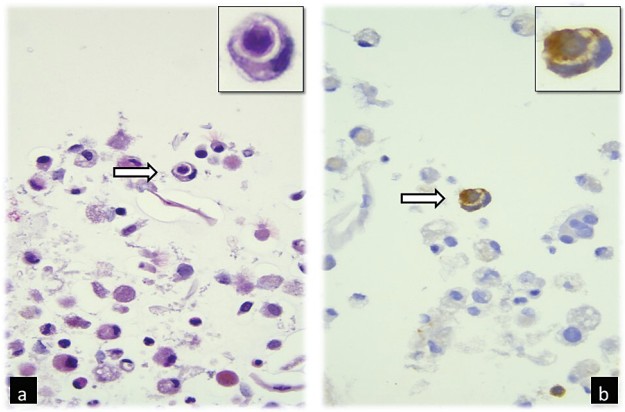

Fig. 2 Broncho-alveolar lavage cell-block photomicrograph showing (**a**) a cannibalistic neoplastic cell with semilunar nucleus and cytoplasm containing the engulfed cell (arrow and insert, H-E, 400×); (**b**) the correspondent positivity for Synaptophysin immunohistochemistry, characteristic of neuroblastoma (arrow and insert, 400×).

analysis might be challenging. The differential diagnosis of small blue round cell tumors in cytology can be broad, necessitating the use of immunohistochemistry to accurately classify the tumor.

The main strength of this report is its demonstration that BAL combined with immunocytochemistry can enable a rapid and minimally invasive diagnosis of NB pulmonary metastasis, even in samples with limited cellularity. However, because it is based on a single case, the report's findings are limited in scope and may not be generalizable to all patients or settings. Further studies are needed to assess the sensitivity and specificity of BAL for this purpose, as well as to define its role compared with other diagnostic methods. Our approach may be restricted to specialized centers with cytopathology expertise. There are still uncertainties regarding the optimal indications for BAL and its diagnostic reliability in cases with very few tumor cells. This highlights areas for future research.

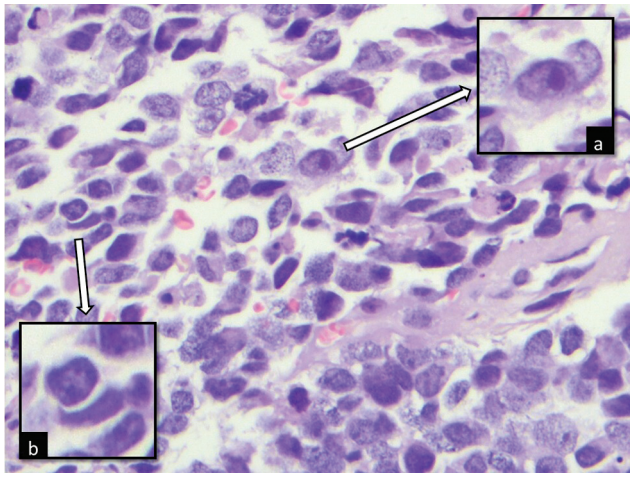

Fig. 3 Histologic photomicrograph showing a neoplastic cell with an enlarged and prominent nucleolus typical of *MYCN*-amplified neuroblastoma (insert a) and a "cannibalistic" neoplastic cell (insert b) (H-E, 400×).

Conclusion

In conclusion, we emphasize the importance of the BAL technique, microscopic characteristics, and immunohistochemical confirmation in diagnosing NB lung metastasis. This case represents the first reported instance of NB lung metastasis diagnosed using BAL, enabling a faster diagnosis and tailored therapy while avoiding more invasive procedures.

Authors' Contributions

S.B.: concept, data acquisition, manuscript preparation, manuscript editing, and manuscript review.
V.G.V.: design, definition of intellectual content, data analysis, statistical analysis, manuscript editing, and manuscript review.
B.C.: clinical studies, experimental studies, data acquisition, and manuscript review.
G.G.: literature search, definition of intellectual content, manuscript preparation, manuscript editing, and manuscript review.
All authors have read and approved the manuscript, meet the requirements for authorship, and believe the manuscript represents honest work.

Patient's Consent

Patient's consent is not required.

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Conflict of Interest

None declared.

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