INSULINOMA-ASSOCIATED PROTEIN 1 (INSM1): IMMUNOCYTOCHEMISTRY ON CYTOLOGY SMEARS IN SMALL CELL CARCINOMA OF LUNG

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Introduction

- Small cell lung carcinoma (SCLC) constitutes approximately 13% of all newly diagnosed lung cancer cases and carry a dismal prognosis
- The majority of SCLC and other pulmonary neuroendocrine tumors are diagnosed on cytology and small biopsy samples
- Immunocytochemistry can improve the accuracy of the diagnosis when used in association with morphologic features
- Chromogranin, synaptophysin, and CD56 are the commonly used cytoplasmic/membranous neuroendocrine (NE) markers with variable sensitivity and specificity
- Due to the cytoplasmic expression, non-specific background positivity frequently occurs in the cytology smears
- About 10% of SCLC are negative or focally positive for these markers, probably due to the absence of overt neuroendocrine differentiation
- An immunohistochemical marker that could combine high sensitivity and specificity with better interpretation would thus be valuable, especially for the diagnosis of SCLC
- INSM1 functions as a transcriptional repressor that controls expression of neuroendocrine phenotype and has recently emerged as a useful diagnostic marker of NE differentiation
- Limited studies have been conducted to evaluate the utility of INSM1 immunohistochemistry in cytologic specimens, however, in cell blocks only
- No prior study has checked for INSM1 immunoreexpression in direct smears

Aims & Objectives

- To evaluate the reliability of INSM1 immunostain on cytology smears in diagnosing pulmonary SCLC
- To correlate immunoreexpression with corresponding surgical pathology specimens wherever available

Methods

- 39 cases of SCLC diagnosed on cytology were retrieved from the departmental archives along with paired biopsies in 12 cases and 24 unmatched biopsies
- 10 cases of non-small cell lung carcinomas (NSCLC) were immunostained as negative control
- Cytology specimens included transbronchial fine-needle aspiration biopsies, bronchial brushings, fine-needle aspiration biopsies from cervical and supraclavicular lymph nodes
- Endobronchial, clot core and lung mass biopsies were included in surgical pathology specimens
- Immunostaining for INSM1 was performed on the smears and surgical specimens
- Nuclear staining was considered positive if there was staining in at least 1% of the neoplastic cells
- Staining was considered focal if less than 50% of the cells were positive

Results

- 32 cases on cytology showed focal to diffuse positivity with strong intensity (sensitivity 94.1%)
- Positive INSM1 staining on cytology was concordant with surgical biopsies in all paired cases
- Two cases were negative on cytology
  - One showed concordant negativity on biopsy
  - Other had no tissue in the block for further staining
- Three other cases did not show viable tumor and showed complete necrosis
- In two cases the diagnosis of SCLC was doubtful because of negativity for all NE markers on biopsy
- All the unmatched surgical biopsies displayed focal to diffuse INSM1 staining
- All the cases of NSCLC were negative (specificity 100%)

Discussion

- INSM1 has been shown as superior immunohistochemical marker compared to other conventional NE markers
- INSM1 is a nuclear protein, which is less prone to potential non-specific reactivity and easy to evaluate than cytoplasmic and membranous NE markers
- Valuable for identification of the high-grade NE carcinomas with poorly differentiated morphology that are negative for conventional NE markers in around 10% of the cases
- INSM1 is more sensitive (92-97%) than chromogranin for NE lung neoplasms, is nearly as sensitive as synaptophysin and is less sensitive than CD56
- Specificity of INSM1 (100%) for NE tumors is identical to the specificity of chromogranin and higher than the specificity of synaptophysin and CD56
- Two cases in our study were negative for INSM1 on cytology and three of the smears were limited by abundant necrosis, which may have influenced the result as may happen with other IHC markers

Conclusion

- As the majority of small cell carcinoma of lung are diagnosed on cytology and small biopsy samples, INSM1 can serve as a reliable diagnostic marker with high sensitivity and specificity
- Being a nuclear neuroendocrine marker, its interpretation is easy in cytology smears

References

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