Diagnostic dilemmas in fine needle aspiration cytology of neuroendocrine tumors
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BACKGROUND

• The rapid-on-site evaluation (ROSE) is commonly used to assess the adequacy of fine needle aspiration (FNA) sampling. It allows for preliminary diagnosis, and to decide whether additional material (more needle passes or core biopsy) is needed for ancillary testing (i.e. molecular cultures, flow cytometry, cell block).

• Neuroendocrine tumors consist of a diverse group of neoplasms that arise from neuroendocrine cells throughout the body. The most common locations originate from gastrointestinal tract and the lungs. These neoplasms can have a broad differential diagnosis depending on cytomorphology, and may sometimes be a challenge for cytopathologists due to overlapping features with other entities.

• We describe two cases which had a discrepancy between on-site evaluation and final diagnosis. In addition, we review the difficulties found during the on-site evaluation, in order to illustrate some of the pitfalls in the diagnosis of neuroendocrine tumors.

METHODS

• One endobronchial ultrasound image-guided fine needle aspiration and one CT image-guided fine needle aspiration performed at the University of Texas Medical Branch were reviewed.

• Both cases had ROSE performed by a cytopathologist and a preliminary diagnosis was rendered. ROSE involved examination of 2-3 Romanowsky stained smears from each FNA pass. Additional 2-3 slides were fixed in 95% alcohol for Papanicolaou staining. The remaining material was fixed in formalin for a cell block preparation.

• Immunohistochemical (IHC) stains were performed in cell block preparations. Morphologic and IHC findings in each case are discussed along with difficulties in the diagnosis.

RESULTS

Case 1: Small cell carcinoma versus lymphoma (Figure 1)

65-year-old male presented to the ER with abdominal pain, dysphagia and hematemesis. He underwent endoscopy, a large esophageal mass was identified, biopsy confirmed an esophageal adenocarcinoma. Additional studies included an endobronchial ultrasound (EBUS) guided FNA of various lymph nodes stations for carcinoma staging.

Romanowsky-stained smears from one lymph node showed numerous cells initially considered as atypical lymphoid cells, with a triad of appearance: moderate cytoplasm and conspicuous nuclei. Cells were discohesive, with crushing artifact and necrosis but no nuclear molding. ROSSE preliminary diagnosis: suspicious for high grade lymphoma. Cell block showed sheets of discohesive cells with enlarged nuclei, incohesive nuclei, fine chromatin, and scant cytoplasm. Immunostains were performed on the cell block. The neoplastic cells were positive for synaptophysin, CD56, and AE1/AE3; and negative for chromogranin, CK7, TTF-1, p40, EMA, and several lymphoid markers. This diagnosis carried a revised of the previous esophageal biopsy, and additional neuroendocrine markers ran confirmed a small cell carcinoma component in the esophageal tumor. In this case the diagnostic dilemma arised with the presence of scattered “blastic” cells without molding, rather than typical cells with “salt and pepper” chromatin. Both lymphoma and small cell carcinoma can show crust artifact, discohesive cells and hyperchromatic nuclei with scant cytoplasm. The role of IHC stains is crucial in such situations.

Case 2: Difficulties of spindle cell morphology (Figure 2)

77-year-old female with a PMH of sarcoidosis and multiple comorbidities complained of chronic cough. CT images demonstrated a LUL nodule, first described on 2004 (1.2 cm), increased in size up to 2.4 cm. A CT-guided FNA of the lung nodule was performed. ROSE smears showed a proliferation of bland spindle cells in loose clusters or as single cells, no mitoses or necrosis. Preliminary diagnosis: spindle cell lesion, with a low grade mesenchymal neoplasm, and less likely, a reactive granulomatous lesion (given patient’s history) in the differential. Cell block revealed clusters of neoplastic cells similar to those seen on smears. Core biopsy stains showed scant cytoplasm, along with fibrous tissue, hemorrhage and chronic inflammation. GMS and Acid fast stains performed on core biopsy due to focal cluster of histiocytes was seen, were negative. Based on our preliminary diagnosis, a large panel of immunostains were performed on cell block. AE1/AE3, EMA and TTF-1 were positive. A carcinoid tumor, spindle cell type was considered, given the indolent nature of this lung standing lung nodule and the TTF-1 positivity. The neoplastic cells were positive for synaptophysin and chromogranin. Desmin, SMA, S100, ALK-1, CD99, p40 carcinoim and CD31 were all negative. The ki-67 less than 1%. Final diagnosis: well differentiated neuroendocrine tumor, consistent with spindle cell carcinoid tumor.

CONCLUSIONS

• Careful examination of cytological features is necessary due to the wide differential diagnosis of neuroendocrine (NE) tumors.

• IHC stains, easily performed on cell blocks, are many times crucial for definitive diagnosis of NE tumors.

• Keep on mind spindle-cell carcinoid tumors in the differential diagnosis of spindle cell neoplasms of the lung.

REFERENCES

