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ThinPrep® General Cytology

History: 68 Year Old - Single mass in the head of the pancreas and multiple liver masses.

Specimen types: Fine Needle Aspirate of Pancreas and Fine Needle Aspirate of Liver

This case was provided by Professor Adalberto Vecchi, MD of Torrette Hospital in Ancona, Italy.

*The images, analysis and diagnosis for this case study were provided to Cytyc by an independent physician. All conclusions and opinions are those of Torrette Hospital and not Cytyc Corporation.

Slide Description:

Slides 1 and 2 have been photographed from the Fine Needle Aspirate of the Pancreas. The background in each picture is composed of predominantly plasmacytoid cells with fragile cytoplasm and prominent nucleoli. These cells are arranged both singly and in small clusters. Rare, large pleomorphic cells are also seen.

Slide 3 is a view of the Fine Needle Aspirate of the Liver from 20x. It shows an identical pattern to the one seen in the aspirate from the pancreas. The pattern is monotonous, with occassional larger cells present which are often bi/multinucleated.

Slide 4 shows another picture taken from the liver aspirate. Clearly recognized under 40x are normal hepatocytes, complete with intranuclear inclusion. Notice, again, the monomorphic population of malignant plasmacytoid cells peppering the background.

Diagnosis: Islet Cell Tumor of the Pancreas, with metastasis to the liver.

The term "Pancreatic Endocrine Neoplasm" (PEN) refers to a group of embryologically related disease processes that includes Islet Cell Tumor, Carcinoid Tumor and Small Cell Carcinoma. These tumors tend to arise in the body and tail of the pancreas, as their precursors (Kulchitsky Cells in Small Cell and Carcinoid Tumors and the Islets of Langerhans in Islet Cell Carcinoma) are concentrated there. They are most common in adult females in their sixth decade. Many patients (as many as 85%) who have inherited the trait for Type I Multiple Endocrine Neoplasia (MEN) Syndrome develop PEN. As in the case discussed here, many patients will present with both the primary pancreatic mass as well as multiple liver metastases, causing the clinician to sample both at aspiration.

Small Cell Carcinomas can be easily distinguished from Islet Cell and Carcinoid Neoplasms due to the presence of the classic morphologic features associated with Small Cell Carcinoma. These characteristics typically include a population of small blue cells with scant cytoplasm and prominent nuclear molding. Many experts believe that differentiating between a pancreatic Carcinoid Tumor and an Islet Cell Tumor can be much more challenging, if not cytologically impossible, as their morphologic features and their immunologic characteristics are very similar. Both may produce clinical evidence of hormone production, as well as share common sites of metastasis. Predicting the behavior of these neoplasms may also be a task that cannot be accomplished through the evaluation of cytologic criteria alone.

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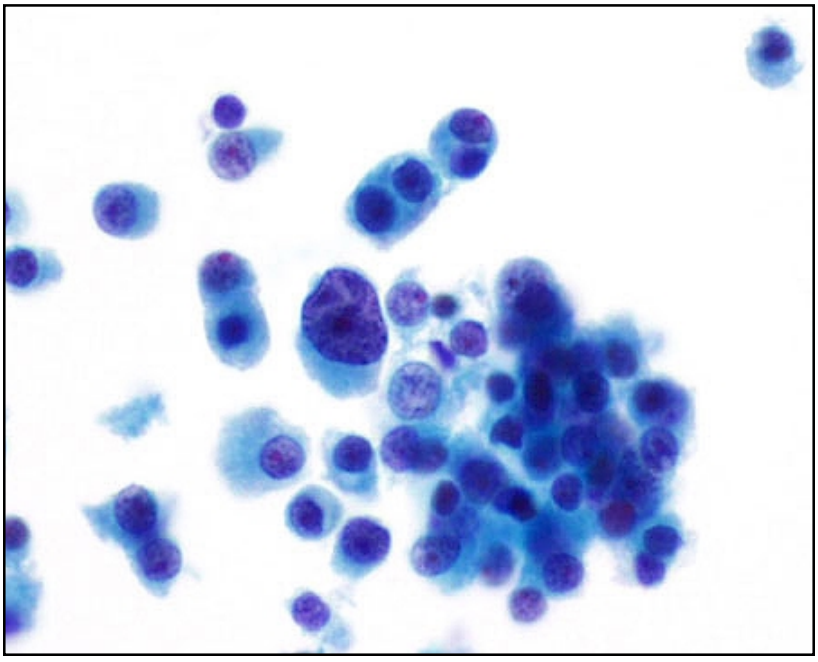
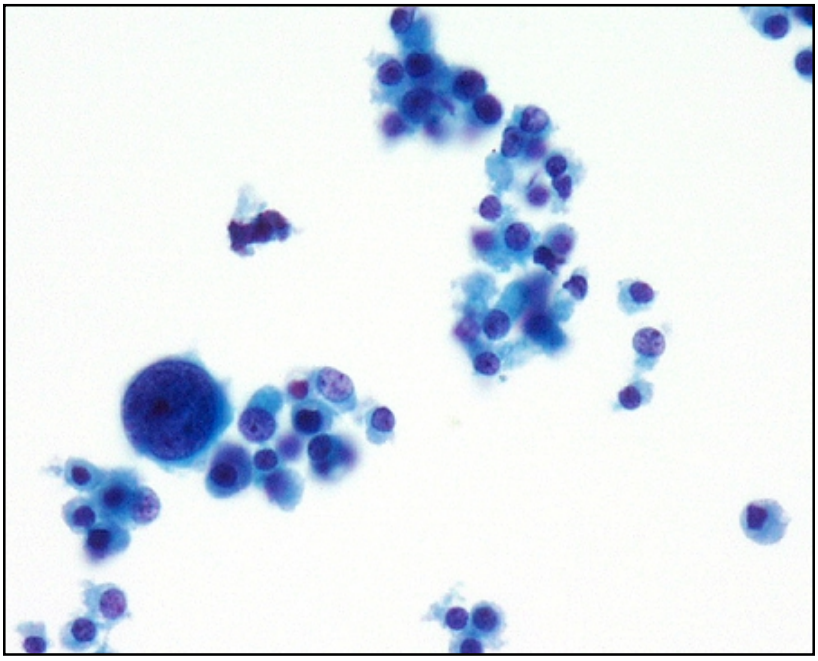


Slide 1 - 60x



Slide 2 - 60x

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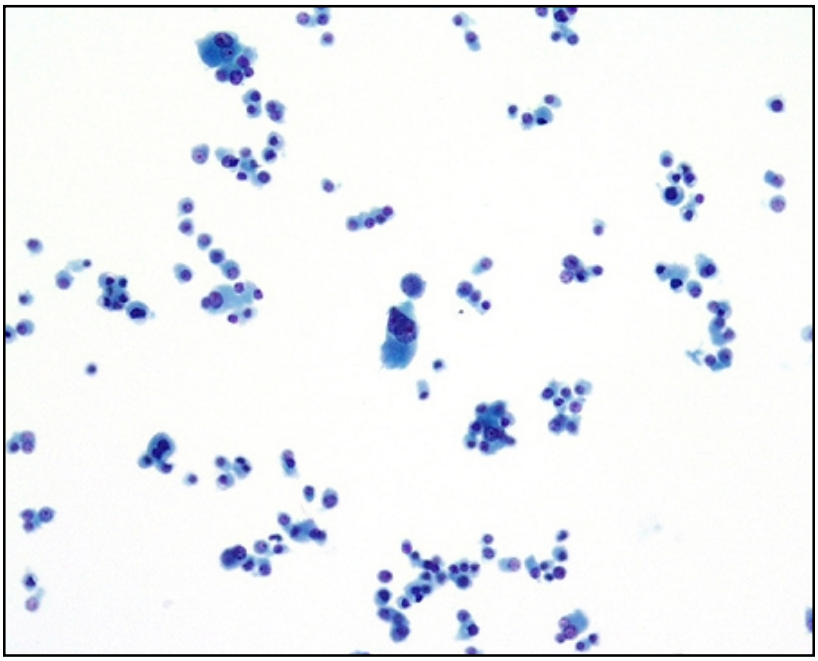
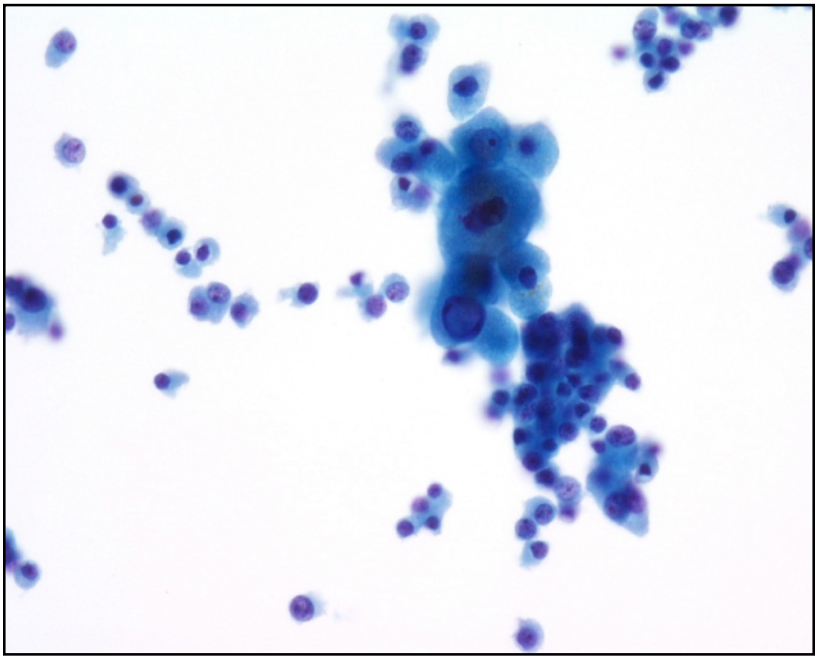


Slide 3 - 20x



Slide 4 - 40x

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Carcinoid tumors of the pancreas and Islet Cell neoplasms share the following cytologic characteristics:

1.) A monotonous pattern of small cells distributed singly, in loosely arranged small clusters, and rosettes.

2.) Finely granular, scant, delicate cytoplasm.

3.) Small, eccentrically placed nuclei that are round to oval in shape with a fine to "salt and pepper" chromatin pattern.

4.) Small nucleoli are common.

5.) Presence of rare, large, multinucleated cells.

Islet Cell Tumors, when actively producing hormones, may cause clinical syndromes such as Diabetes Mellitus (somatostatin or glucagon), Zollinger-Ellison Syndrome (gastrin) and Verner-Morrison Syndrome (vasoactive intestinal polypeptide), to name a few. Immunostaining for a specific secretory product may be helpful in the differentiation of Islet Cell and Carcinoid tumors.

As for predicting the biological behavior of these tumors, statistics show that a vast majority of non-functioning tumors is malignant. Many believe that the only reliable indicator of malignancy is the presence of metastatic disease. However, Bibbo and DeMay have both suggested that there may be cytologic features of Islet Cell neoplasms that suggest malignancy, especially when present in their entirety. These criteria include:

1.) An overall increase and variability in the nuclear size, as well as the size of the entire cell.

2.) Multinucleated pleomorphic cells.

3.) Mitotic figures.

4.) Necrosis or tumor diathesis.

Treatment strategies vary greatly, dependent upon the behavior and metabolic characteristics of the tumor, as well as the extent of disease. The only absolute cure involves surgical intervention, when feasible. If the tumor is inoperable, other modalities such as radiation, chemotherapy and anti-hormonal drugs may be employed to bring about significant palliation of clinical symptoms, as well as improve survival.

References:

1.) DeMay, R: The Art and Science of Cytopathology. 1996: 1066-68, 1077.

2.) Bibbo, M: Comprehensive Cytopathology. 1997: 858-60.

3.) Ramzy, I: Clinical Cytopathology and Aspiration Biopsy: Fundamental Principles and Practice. 2001: 309-10, 317.

4.) Koss, LG, Woyke, S, Olszewski, W: Aspiration Biopsy: Cytologic Interpretation and Histologic Bases. 1992: 557, 581-85.

5.) Silverman, JF, Atkinson, BF: Atlas of Differential Diagnoses in Cytopathology. 1998: 331-34.

6.) WebMD. Islet Cell Cancer Treatment Information for Health Professionals.