December 2021

Missouri Cancer Registry and Research Center
Show-Me-Tips

Coding...Abstracting...Education…

Ed 21:03
NET

NEUROENDOCRINE TUMORS

Neuroendocrine tumors (NETs) are relative newcomers to medical recognition, carcinoid tumors were first identified as a specific, distinct type of growth in the mid 1800's, and the name "carcinoid" was first applied in 1907 by Oberndorfer in Europe in attempt to designate these tumors as midway between carcinomas and adenomas.

They were found to arise from the cells of the Diffuse Neuroendocrine System, enterochromaffin cells (glandular endocrine-hormone producing cells) widely distributed in the body but found in greatest amounts in the small intestine and then in decreasing frequency in the appendix, rectum, lung, pancreas and very rarely in the ovaries, testes, liver, bile ducts and other locations. These cells have special peculiar features that make them identifiable under the microscope. They stain in a special way when put in contact with silver containing chemicals. Special stains for the particular hormones that enterochromaffin cells can make will identify the hormone substances in carcinoid tumor cells and thereby confirm the diagnosis of the microscopic exam on biopsied carcinoid tumors.

https://www.carcinoid.org/for-patients/general-information/a-review-of-carcinoid-cancer/

Types of Neuroendocrine Tumors (NETS)

GI NETS
- Well differentiated NET
- Neuroendocrine *carcinoma*

Lung NETS
- Typical
- Atypical
- Large Cell
- Small Cell

NAACCR Webinar: NET May 2019

Pancreatic NETS (pNETS)
- Well differentiated pNETS
- Poorly differentiated pancreatic neuroendocrine *carcinoma*
- Funtional pNETS
  - Gastrinoma
  - Insulinoma
  - Glucagonoma
  - Somatostatinoma
  - VIPoma
  - ACTHoma

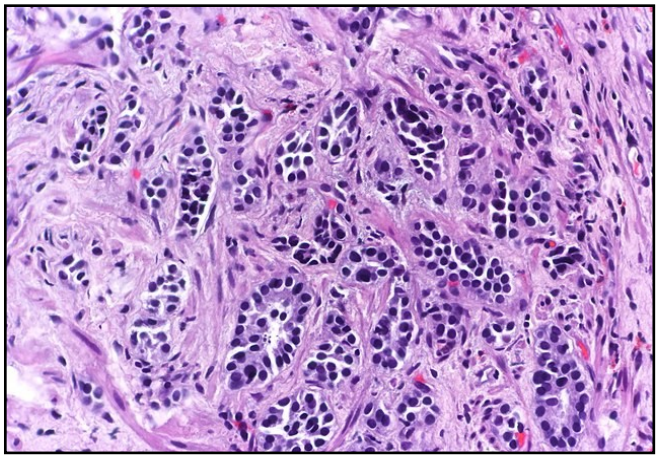
There are also some very unusual and extremely rare locations from which carcinoids may arise or to which they have spread and they are:
the gallbladder and bile ducts, the ovaries, the testicles, the urinary bladder, the prostate gland, the breast, the kidneys and the thymus gland and in some very rare cases of the eye and the ear.

https://www.carcinoid.org/for-patients/general-information/a-review-of-carcinoid-cancer/

Well Differentiated, NET

8240/3 Well differentiated neuroendocrine tumor G1
8249/3 Well differentiated neuroendocrine tumor G2
8240/3 Well differentiated neuroendocrine tumor G3

8246/3 Neuroendocrine carcinoma



WD Neuroendocrine Tumor of the Stomach
https://commons.wikimedia.org/wiki/File:Well-differentiated_neuroendocrine_tumor_of_the_stomach,_very_high_mag.2.jpg

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Approximately 20% (1/5) of the small intestine carcinoids will develop distant spread (metastases) and roughly 1/3 of those that have spread will develop symptoms of the Carcinoid Syndrome. Carcinoid Syndrome is very rare.

https://www.mayoclinic.org/diseases-conditions/carcinoid-tumors/symptoms-causes/syc-20351039

What Is Carcinoid Syndrome?

Carcinoid cells can make hormones. Those carcinoid tumors which produce large amounts of hormones and other potent chemical substances and which are usually found to have spread to the liver, can cause hot red flushing of the face, diarrhea, and asthma like wheezing attacks. These episodes of "carcinoid crisis" may be very infrequent at first but gradually occur more often and are usually associated with abrupt low blood pressure & even fainting. After a while the flush may become persistent in some individuals and may not be felt or noticed by them. The diarrhea may also be chronic and weight loss can occur. All of these features constitute the Carcinoid Syndrome.

An inherited familial (genetic) condition can cause the development in an individual of several different types of neuroendocrine tumors (and their respective syndromes). This can include carcinoid along with other types of neuroendocrine tumors. This is called MEN (multiple endocrine neoplasia) syndrome.

https://www.carcinoid.org/for-patients/general-information/a-review-of-carcinoid-cancer/

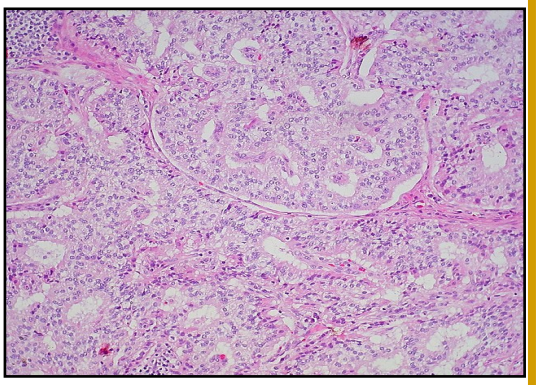
Familial syndromes

Most pancreatic NETs are sporadic. However, neuroendocrine tumors can be seen in several inherited familial syndromes, including:

- multiple endocrine neoplasia type 1 (MEN1)
- multiple endocrine neoplasia type 2 (MEN2)
- von Hippel-Lindau (VHL) disease
- neurofibromatosis type 1
- tuberous sclerosis
- Carney complex

Given these associations, recommendations in NET include family history evaluation, evaluation for second tumors, and in selected circumstances testing for germline mutations such as for MEN1.

https://en.wikipedia.org/wiki/Neuroendocrine_tumor



WD Neuroendocrine Tumor of the Duodenum
https://commons.wikimedia.org/wiki/File:Well-differentiated_neuroendocrine_tumor_of_the_duodenum_(3048456334).jpg

Gastrointestinal carcinoid tumors form from a certain type of neuroendocrine cell . These cells are scattered throughout the chest and abdomen but most are found in the GI tract. These neuroendocrine cells make hormones that help control digestive juices and the muscles used in moving food through the stomach and intestines. A GI carcinoid tumor may also make hormones and release them into the body.

Carcinoids, primarily some midgut carcinoids, secrete excessive levels of a range of hormones, most notably serotonin (5-HT) or substance P, causing carcinoid syndrome.

https://www.cancer.gov/types/gi-carcinoid-tumors/patient/gi-carcinoid-treatment-pdq#_1

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NEUROENDOCRINE TUMORS

Risk factors for GI carcinoid tumors include the following:

- Having a family history of multiple endocrine neoplasia type 1 (MEN1) syndrome or neurofibromatosis type 1 (NF1) syndrome.
- Having certain conditions that affect the stomach's ability to make stomach acid, such as atrophic gastritis, pernicious anemia, or Zollinger-Ellison syndrome.

https://www.cancer.gov/types/gi-carcinoid-tumors/patient/gi-carcinoid-treatment-pdq#_1

Medullary thyroid cancer

Medullary thyroid cancer begins in thyroid cells called C cells, which produce the hormone calcitonin. Elevated levels of calcitonin in the blood can indicate medullary thyroid cancer at a very early stage. Certain genetic syndromes increase the risk of medullary thyroid cancer, although this genetic link is uncommon.

https://www.mayoclinic.org/diseases-conditions/thyroid-cancer/symptoms-causes/syc-20354161

Merkel cell carcinoma

Merkel cell carcinoma is a rare type of skin cancer that usually appears as a flesh-colored or bluish-red nodule, often on your face, head or neck. Merkel cell carcinoma is also called neuroendocrine carcinoma of the skin.

It's not clear what causes Merkel cell carcinoma. Merkel cell carcinoma begins in the Merkel cells. Merkel cells are found at the base of the outermost layer of the skin (epidermis). Merkel cells are connected to the nerve endings in the skin that are responsible for the sense of touch.

Researchers recently discovered that a common virus plays a role in causing most cases of Merkel cell carcinoma. The virus (Merkel cell polyomavirus) lives on the skin and doesn't cause any signs or symptoms. Just how this virus causes Merkel cell carcinoma has yet to be determined. Given that the virus is very common and Merkel cell carcinoma is very rare, it's likely that other risk factors play a role in the development of this cancer.

https://www.mayoclinic.org/diseases-conditions/merkel-cell-carcinoma/symptoms-causes/syc-20351030

ICD-O 3.2 NET Coding Updates

2014

8240	New related term New related term New related term	Neuroendocrine tumor, grade 1 Neuroendocrine carcinoma, low grade Neuroendocrine carcinoma, well differentiated
8249	New related term New synonym	Neuroendocrine carcinoma, moderately differentiated Neuroendocrine tumor, grade 2
8244	New related term New synonym	Mixed adeno-neuroendocrine carcinoma MANEC

https://www.naaccr.org/icdo3/

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NEUROENDOCRINE TUMORS

ICD-O 3.2 NET Coding Updates

2018

8041	New term New term	High-grade neuroendocrine carcinoma **(C54._, C55.9)** Neuroendocrine carcinoma, poorly differentiated **(C50. _)**
8246	New term	Neuroendocrine tumor, well differentiated **(C50. _)**

ICD-O 3.2 NET Coding Updates

2021

8150/3	Behavior code change (change in reportability)	Pancreatic neuroendocrine tumor, nonfunctioning **(C25.4)** Reportable for cases diagnosed 1/1/2021 forward.

https://www.naaccr.org/icdo3/

Solid Tumor Rules - Breast

- 8041/3 Neuroendocrine **Carcinoma,** poorly differentiated
- 8246/3 Neuroendocrine **Tumor**, well differentiated

Solid Tumor Rules - Colon/Rectum

8240/3 Neuroendocrine **Tumor** Grade 1

- Well Differentiated Neuroendocrine **Tumor**, G1
- Low Grade Neuroendocrine **Tumor**
- NET G1
- Carcinoid, NOS

Subtypes

- 8249/3-Neuroendocrine **Tumor** Grade 2
- 8156/3-Somatostatin-producing NET
- 8241/3-EC cell serotonin-producing NET/ enterochromaffin cell carcinoid

8246/3 Neuroendocrine ***Carcinoma (NEC)***

- 8013/3 Large Cell NEC
- 8041/3 Small Cell NEC

NAACCR Webinar: NET May 2019

Breast NET Histology:

A patient was found to have a single tumor in their **breast**. The tumor was resected.

Pathology showed:
Well differentiated neuroendocrine tumor

What histology would be assigned?

- Rule H14 of the Solid Tumor Rules - Breast tells us to code the histology when only one is present and refers us to Table 3
- Table 3 tells us to code the histology to **8246/3**

Colon NET Histology:

A patient was found to have a single tumor in their **sigmoid colon**. The tumor was resected.

Pathology showed:
Well differentiated neuroendocrine tumor, G1

What histology would be assigned?

- Rule H9 of the Solid Tumor Rules - Colon tells us to code the histology when only one in present and refers us to Table 1
- Table 1 tells us to code the histology to **8240/3**

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NEUROENDOCRINE TUMORS

Solid Tumor Rules Lung

- 8041/3 Neuroendocrine **Tumor**
- 8013/3 Large cell neuroendocrine **carcinoma**/ combined large cell neuroendocrine carcinoma
- 8249/3 Atypical Carcinoid
- 8240/3 Typical Carcinoid

Solid Tumor Rules Urinary Sites

8041/3 Small cell neuroendocrine **carcinoma**

NAACCR Webinar: NET May 2019

Rectal NET Grade:

A patient had a rectal biopsy which showed **High Grade Neuroendocrine carcinoma.**

The tumor was resected.

Pathology showed:
High Grade Neuroendocrine carcinoma.

Mitotic Rate 12. Ki-67 > 90%

Neuroendocrine tumor grades are based on the mitotic rate and the Ki-67. When the Mitotic Rate is greater than 12 and Ki-67 is greater than 90. This fits the definition for Grade 3.

G3: Mitotic count (per 10 HPF) greater than 20 OR Ki-67 index (%) greater than 20

What is Clinical Grade?
Clinical Grade is D
(if the only information you have is "high grade" you can use the generic guidelines for coding grade)

What is Pathological Grade?
Pathological Grade is 3

https://cancerbulletin.facs.org/forums/forum/site-specific-data-items-grade-2018/90625-colon-grade#post91026

Lung NET Histology:

A patient was found to have a single tumor in their **lung.** The tumor was resected.

Pathology showed: **Neuroendocrine tumor**

What histology would be assigned?

- Rule H4 of the Solid Tumor Rules - Lung tell us to code the histology when only one is present and refers us to Table 3
- Table 3 tells us to code the histology to **8041/3**

Pancreas NET Histology:

A patient was found to have a single tumor in their **pancreas**. The tumor was resected.

Pathology showed:
Neuroendocrine tumor, G1

What histology would be assigned?

- The 2018 ICD-O Updates Table does not include this term
- The 2014 ICD-O Updates Table tells us to code this **8240/3**

Colon NET Grade:

A patient had a small bowel biopsy which showed **Well Differentiated Neuroendocrine Tumor, G2**

The distal ileum and cecum were resected.

Pathology showed:
Well Differentiated Neuroendocrine Tumor, G1

What is Clinical Grade?
Clinical Grade is 2

What is Pathological Grade?
Pathological Grade is 2

https://cancerbulletin.facs.org/forums/forum/site-specific-data-items-grade-2018/117602-high-grade-net-post-therapy

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NEUROENDOCRINE TUMORS

Canswer Forum update 6/14/21 NET of gastrointestinal morphologies

"Well-differentiated neuroendocrine carcinoma," can be a Grade 1, 2, or 3 based on the mitotic rate and/or Ki-67.
If the pathologist documents the grade as Grade 1 (G1), Grade 2 (G2) or Grade 3 (G3) then you can code it 1, 2 or 3.

Code	Grade Description	
1	G1: Mitotic count (per 10 HPF) less than 2 AND Ki-67 index (%) less than 3	Preferred grading system
2	G2: Mitotic count (per 10 HPF) equal 2-20 OR Ki-67 index (%) equal 3-20	
3	G3: Mitotic count (per 10 HPF) greater than 20 OR Ki-67 index (%) greater than 20	
A	Well differentiated	Generic grade codes
B	Moderately differentiated	
C	Poorly differentiated	
D	Undifferentiated, anaplastic	
9	Grade cannot be assessed (GX); Unknown	

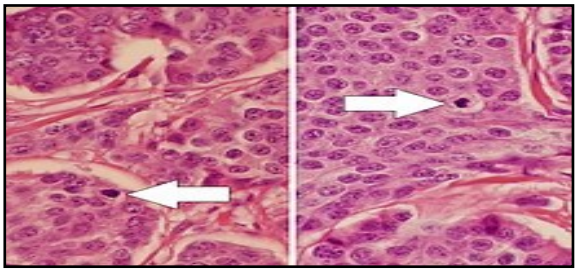
https://apps.naaccr.org/ssdi/list/

Grade 1 – NET G1 (8240/3)
Grade 2 – NET G2 (8249/3)
Grade 3 – NET G3
Grade 1 – neuroendocrine carcinoma, low grade (8240/3) or neuroendocrine carcinoma, well differentiated (8240/3)
Grade 2 – neuroendocrine carcinoma, moderately differentiated (8249/3)
Grade 3 – neuroendocrine carcinoma, poorly differentiated

But if the pathologist documents "Well-differentiated neuroendocrine carcinoma" with **no** documentation of G1, G2, or G3 then you cannot use the preferred grading system. You would have to assign "A" from the generic grade codes, since it is identified as a well-differentiated carcinoma.

https://cancerbulletin.facs.org/forums/forum/site-specific-data-items-grade-2018/114449-colon-net-grade#post114497

G1 and G2 neuroendocrine neoplasms are called neuroendocrine tumors (NETs) – formerly called carcinoid tumors. G3 neoplasms are called neuroendocrine carcinomas (NECs).



Mitotes in a Neuroendocrine Tumor
https://en.wikipedia.org/wiki/Neuroendocrine_tumor

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