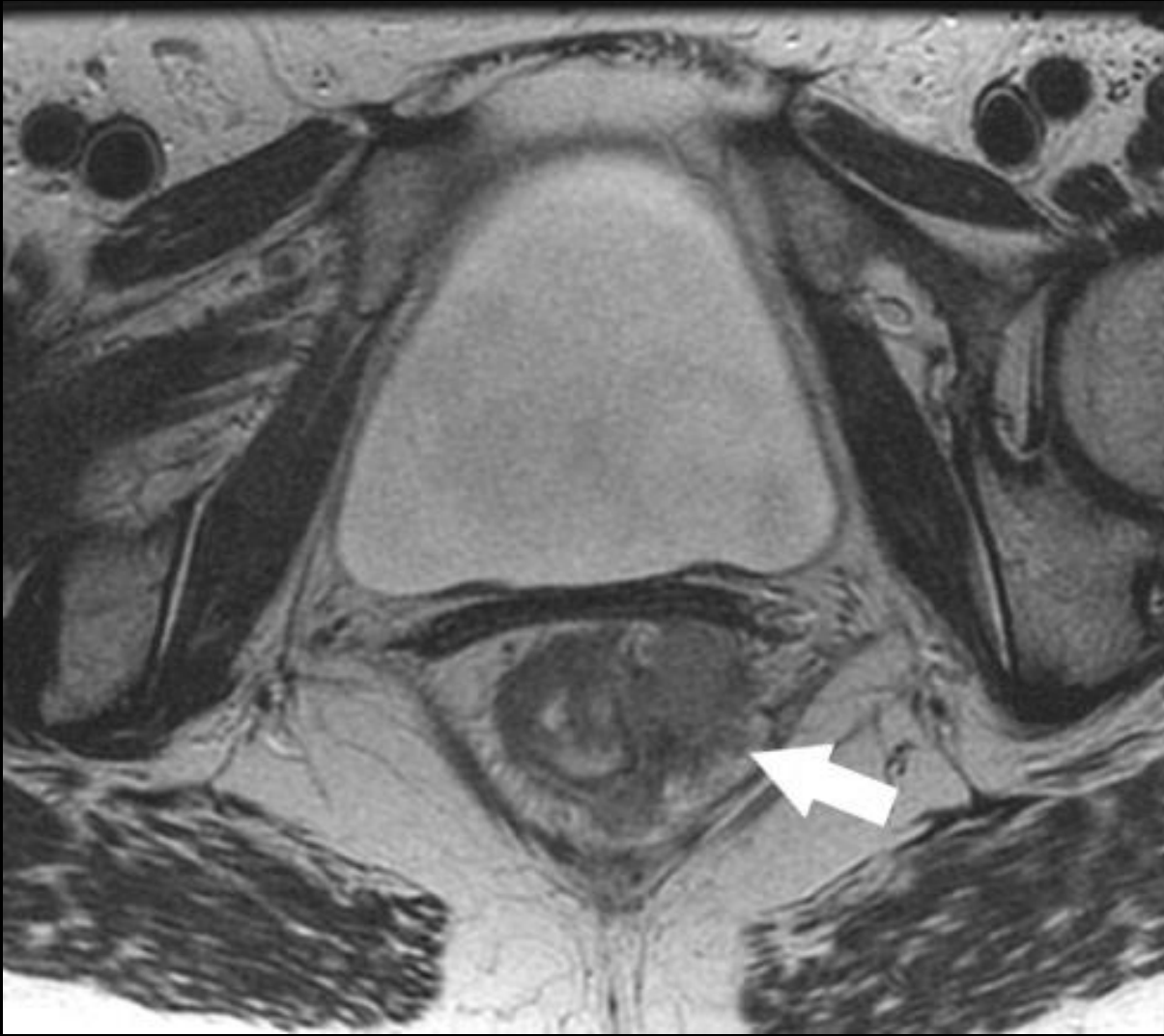


Neuroendocrine Neoplasm of the Rectum

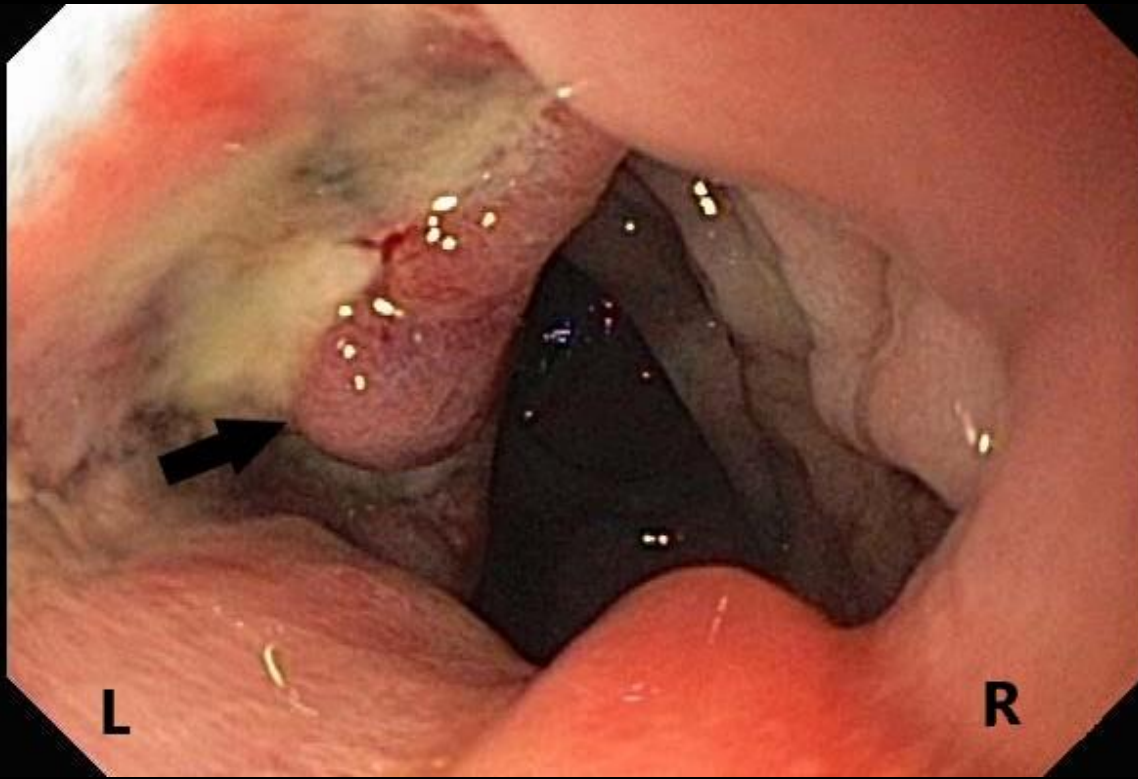
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History

- A 56-year-old female was diagnosed with rectal cancer after undergoing colonoscopy for diarrhea and rectal bleeding.



Axial and coronal T2 weighted MRI images demonstrate a primary rectal mass (white arrow) with extensive local spread of disease including extramural vascular invasion and tumor deposits. A large tumor deposit is outlined with a black arrow.



A photograph from initial endoscopy demonstrates an ulcerated malignant appearing anorectal mass extending to the dentate line. Radial echoendoscope shows a hypoechoic mass that demonstrates a bulky exophytic component (white arrow) extending through serosa into the mesorectal fat.



Axial (left) and coronal (right) T2 weighted MRI images demonstrate a metastatic left superficial inguinal node (black arrow-axial) typical of anal cancers. Tumor spread along the rectal lymphatics (black arrow coronal) is also present. The primary tumor (white arrow) involves both the anal canal and rectum resulting in a dual pattern of spread.

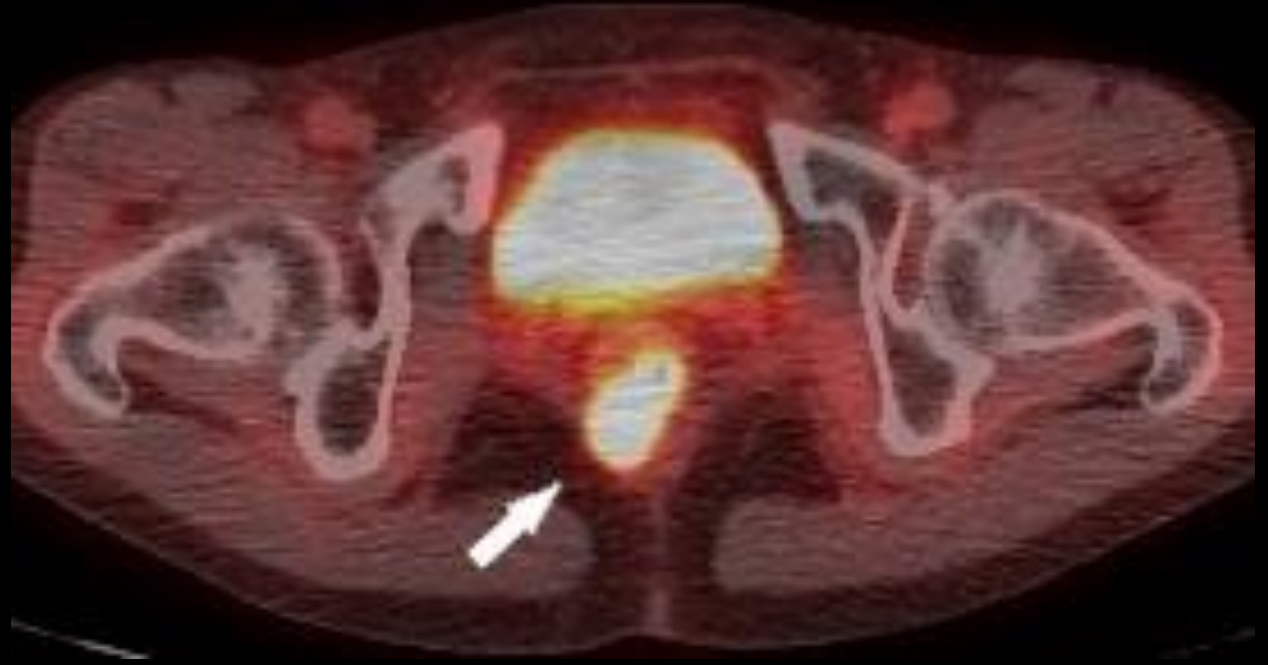
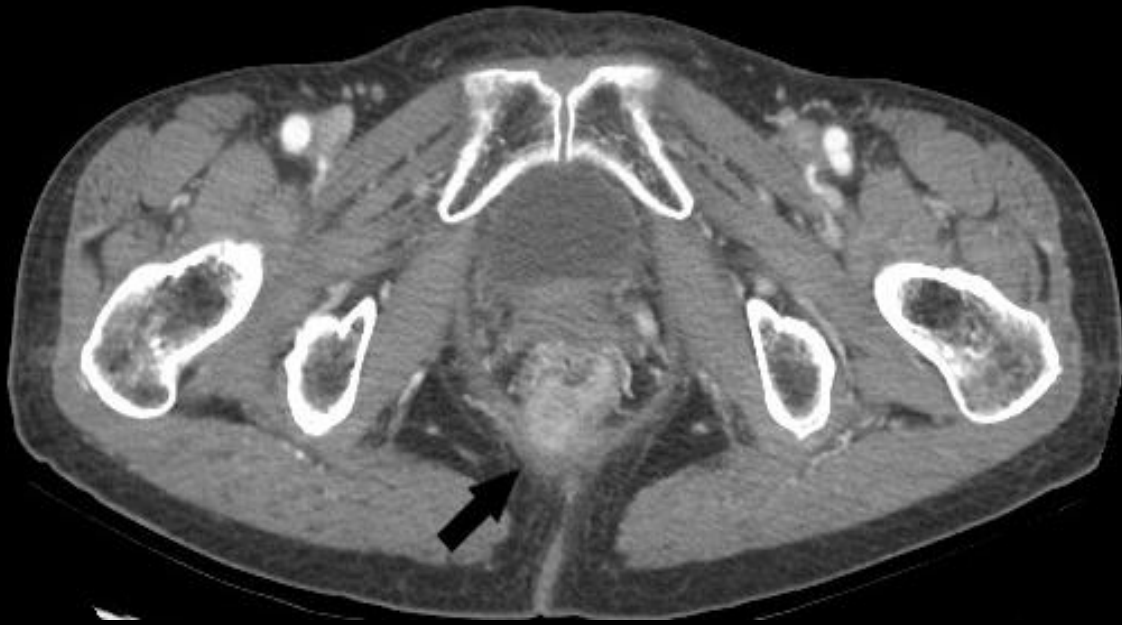


Baseline contrast enhanced axial CT scan (left image) demonstrates no liver metastases. On follow-up CT scan four months later (right image), multiple new hypervascular metastases are present (only a single lesion is shown). Given the extensive EMVI and high tumor grade, rapid progression of metastatic disease is typical.

Clinical course

- Physical exam: a bulky mass at the anal verge occupying ~ 50% of the lumen.
- Pelvic MRI : an invasive tumor with left superficial inguinal and bulky metastatic mesorectal adenopathy, extramural vascular invasion and tumor deposits. No distal metastatic disease was present on the initial CT scan.
- Biopsy revealed a high-grade neuroendocrine carcinoma with small cell features.
- Treatment: 3 months of pre-irradiation cisplatin plus etoposide chemotherapy. The patient progressed and was started on weekly paclitaxel therapy with palliative external beam radiation therapy.
- The patient expired approximately six months after her diagnosis.

Companion case



A second patient with a high grade R-NEN demonstrates an enhancing mass on CT scan (black arrow). The corresponding FDG-PET scan demonstrates the FDG avid tumor with $SVU=27$ (white arrow).

Companion case



A third patient with an invasive intermediate grade neuroendocrine neoplasm. A contrast enhanced CT scan demonstrates a suspicious mesorectal node (white arrow) and a corresponding fused 68Ga-DOTATATE PET/CT demonstrates avid uptake (blue arrow) with SVU=70.

Discussion

- Gastrointestinal neuroendocrine neoplasms (NEN) have been significantly increasing in incidence and prevalence over the past two decades.
- Rectal NENs (R-NENs) have shown the greatest rate of increase with an incidence of 1.04/100,000 cases per year.
- The median age at diagnosis is 56 years with a M:F ratio of 1.1. They occur more frequently in blacks and Asians.
- They develop from the muscularis mucosa or the submucosal layer rather than the mucosa.

Discussion

- Risk factors include high cholesterol, ferritin, presence of metabolic syndrome and family history.
- 2-40% NENs are associated with a multiple endocrine neoplasia 1 gene mutation. For most tumors, no causation is identified.
- The survival depends on the size and degree of differentiation.
The 2022 WHO grading system subclassifies NEN into:
 - Low to intermediate grade G1-G3 neuroendocrine tumors (NETs).
 - High grade neuroendocrine carcinomas (NECs), either small cell or large cell.
 - The Ki-67 index of G3 NET and NEC is greater than 20%.
- Poorly-differentiated neuroendocrine carcinomas, such as in this case, are most commonly small cell carcinomas. This is one of the most aggressive rectal tumors and dissemination and rapid clinical deterioration are common.

Clinical Features – Tumor marker

- Low grade R-NEN tumors are usually asymptomatic, discovered more frequently with screening colonoscopy. 80-90% of tumors are detected when they are confined to the submucosa and are less than 1 cm, with an overall five-year survival of 93%.
- Serum Chromogranin A can be used in many neuroendocrine tumors but is of limited use in non-metastatic R-NENs. It can be useful for monitoring patients with metastatic disease or for surveillance in patients with resected tumors.

Anatomic Imaging

- R-NENs >1 cm in size or with high-risk features should undergo pelvic MRI and/or endorectal ultrasound (EUS) to determine depth of invasion and lymph node status.
 - On rectal ultrasound, these appear as hypoechoic or isoechoic lesions and the depth of invasion can be accurately measured.
- For rectal NENs >2 cm, with invasion beyond submucosa, or with positive lymph nodes, the North American Neuroendocrine Tumor Society (NANETS), the European Neuroendocrine Tumor Society (ENETS), and the National Comprehensive Cancer Network (NCCN) guidelines recommend CT or MRI of the abdomen and pelvis. Full colonoscopy should also be performed.

Anatomic Imaging

- MRI : small R-NENs appear as superficial submucosal masses with contrast enhancement. They may be similar to adenocarcinomas and demonstrate ulcerations.
 - Typically isointense on T1WI and iso- to hyperintense on T2WI relative to muscle.
 - DWI sequences have the highest sensitivity in detection of NENs and metastases.
- CT: majority of NENs are hypervascular, but many are non-hypervascular . NEN vascularity is inversely proportional to its grade.
 - The primary role of CT is to detect regional and distant metastases, not assess primary mass
 - CT has a reported mean detection rate for liver metastasis of 81% in NENs, lower than MRI and Ga-68 DOTATATE PET/CT.

Functional Imaging

- Like other NENs, somatostatin receptor (SSTR DOTATATE and DOTATOC) PET imaging with CT or MRI is used for localization of SSR-positive R-NEN.
- Ga-68 DOTATATE has highest accuracy of 97% in detection of NENs.
- SSTR imaging has also been used for staging and restaging and to select patients for peptide receptor radionuclide therapy (PRRT) with cold or radiolabeled somatostatin analogs.

Management

- For tumors < 1 cm, local resection is recommended by both NANETS and ENETS.
 - Less than 2% are associated with lymph node spread and 0.7% are associated with distant metastases.
- The method of local resection can be either endoscopic or transanal surgery.
- Several endoscopic procedures can be used to remove small NENs including conventional polypectomy, endoscopic mucosal resection and endoscopic submucosal dissection depending on the depth of invasion.
- For metastatic disease treatment options include somatostatin analogs, interferon, systemic chemotherapy, peptide receptor radiotarget therapy, and locoregional and ablative procedures.

Conclusion

- Rectal NENs currently comprise the majority of the GI NENs.
- Survival in these cases depends on the size and degree of differentiation.
- Anatomic as well as functional imaging play an important role in triaging these cases for appropriate management.

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