Neuroendocrine Tumours (NETs)
An introduction

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Neuroendocrine Tumours (NETs)

- Rare group of tumours derived from secretory cells (GIT, lung etc.)
- Most come from gastrointestinal tract (carcinoid)
- Incidence appears to be increasing 3-5/100,000 pa
- Unfortunately often misdiagnosed or overlooked in diagnosis
- 60% have spread at diagnosis
Location of NETs

- **Gastric carcinoid**
  - Zollinger – Ellison syndrome; ↑ gastrin level
  - Peptic ulcer disease

- **Foregut carcinoid**
  - Bronchus, stomach; 1st part of duodenum, pancreas and ovaries
  - Can secrete a number of hormones (GH, ACTH)

- **Midgut carcinoid**
  - 2nd portion of the duodenum; jejunum; ileum; right colon
  - Secretes serotonin, prostaglandins and substance P
  - Classically produce carcinoid syndrome

- **Hindgut carcinoid**
  - Transverse colon; left colon/sigmoid; rectum
  - Rarely secrete hormones and hence clinically silent
Associated Conditions

- Von Hippel Lindau

- Multiple endocrine neoplasia syndromes (MEN)
  - pheochromocytomas
  - carcinoma of thyroid
  - parathyroid disease

- Von Recklinghausen disease

- Neurofibromatosis

- Tuberous sclerosis
Diagnosis is complex – relying on a high index of suspicion by physician and many radiological and laboratory tests.

The treatment for metastatic disease is multi-modal – surgery; combination chemotherapy; hormonal manipulation (somatostatin analogues); radionuclide; interferon.

Early diagnosis before tumour spread can allow for curative surgical resection of the primary.
Characteristics of NETs

- Rare,
- Usually small <1cm
- Slow growing

- Usually metastasize to liver before becoming symptomatic; often when primary tumour is >2cm

- Episodic clinical symptoms; may be ‘silent’ for many years

- Often misdiagnosed as symptoms may mimic common conditions
Carcinoid Tumours

- The most common of the gut endocrine tumours – account for 15-30% of small bowel tumours
- Can occur in the bronchus, pancreas, rectum, ovary, lung
- Derived from enterochromaffin cells which secrete serotonin (5-HT)
Carcinoid Syndrome

- Occurs in less than 10% of patients with carcinoid. More common with tumours of small bowel (midgut)

- Vague abdominal pain (intermittent); diarrhoea; flushing; heart lesions; cramps; wheezing; arthropathy and myopathies.
Biochemical Markers

- **Chromogranin A**
  - A protein released from the enterochromaffin cells with other hormones
  - Absolute levels not important but trend is

- **Synaptophysin**

- **Ki-67; proliferative index; mitotic rate**

- **Serotonin breakdown products**
  - 5-hydroxyindoleacetic acid (5-HIAA) in urine

- **Gastrin, serotonin, pancreatic polypeptide**
Imaging Modalities

- Contrast CT
- MRI
- Angiography
- Ultrasound
- Invasive – ERCP; gastroscopy; colonoscopy
Functional and Radioisotope Scanning

- $^{111}$Indium labelled octreotide (Octreoscan) – binds to somatostatin receptors on NETs and taken up into cell → high affinity, responsive to somatostatin analogues

- Fluorodeoxyglucose PET (FDG-PET) – increased affinity for high Ki-67 lesions (inversely related to somatostatin affinity)

- $^{68}$Gallium labelled octreotide PET/CT – new gold standard in nuclear medicine imaging for NETs
Treatments

- Surgery

- Somatostatin analogues for octreotide-avid, slow growing asymptomatic tumours

- Chemotherapy – Streptozotocin +/- 5-FU; doxorubicin; cisplatin/carboplatin; temozolomide and other novel agents such as anti-vascular growth factor – Avastin

- Radiolabelled peptides – $^{111}$Indium, $^{90}$Yttrium, $^{177}$Lutetium
Where next?

- Support and be supported

- Unite with other sufferers to ensure the best delivery of care, hopefully with the assistance of the Unicorn Foundation as advocacy

- Don’t settle for “I don’t know…”