MEN 1 GEP Tumours

Pancreatico-Nodal (-Duodenal)

Affects 35-80% of MEN1 patients

Functioning or non functioning

Hyperplasia  microadenoma  macrotumours

Solid or cystic

50% malignant (well / poorly differentiated)

Progression is slow

Recurrence is common

Diagnosis – abnormal morphology and /or abnormal biochemistry
Treat the hormonal and the tumour syndromes
## MEN-1 Monitoring Sheet

**Mutation:**
- DNA test: YES/NO
- Date:

<table>
<thead>
<tr>
<th>DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
</tbody>
</table>

### Parathyroid
- Corrected calcium (NR 2.20-2.60)
- PTH (NR 8-63)
- Bone Alk Phos
- NTX

### Pancreas
- Gli Peptides
- VIP (NR<50)
- PP ($\sigma R < 300$)
- Gantrin ($\sigma R<40$)
- Glucagon ($\sigma R<50$)
- Somatostatin ($\sigma R<150$)
- Neurotensin ($\sigma R<100$)

### Imaging
- Dexa Score Lumbar Spine and Femoral Neck
- MRI Pituitary
- MRI Pancreas and Adrenals
- Comments and Treatment
MEN 1 Pancreas

Non Functioning Tumours
> 50% patients on screening
>80% patients on histology
RR of Death  3.6
10 year survival 62%

Rare Functioning Tumours
Glucagonoma (1.5%)/Vipoma (1%)/Somatostatinoma (<1%)
10 year survival 53%
MEN 1 Pancreas

Insulinoma

10-33% of functioning GEP
20% patients on histology
Very rare in head of pancreas
>3cm diameter increased risk of malignancy

10 years survival 90%
Gastrinoma

60% of functioning GEP
85% in duodenum
Diagnosis by elevated basal gastrin and secretin test
Exclude metastases by CT and SRS

Significance of nodal disease ??
At duodenal surgery - ≤ 0.5cm enucleate
Remember all duodenum is at risk

10 years survival 80%. RR of Death 2.5
PET in MEN Type 1

“…indications for intervention are controversial…”

Management of Pancreatic Endocrine Tumours in MEN 1

“...current management ...is very much an art as well as a science....”

GEP in MEN 1 – Natural History

Lethality of MEN Type I

Are Patients with MEN Type I Prone to Premature Death?

Do Patients with MEN Syndrome Type 1 Benefit from Periodical Screening?

Nodal disease indicates malignancy not aggressivity
Liver metastases do not necessarily indicate short survival
Screening for GEP in MEN 1
Age at onset?

French GTE Registry > 800 MEN cases

15% ≤ 20 years of age
23% (29 patients) with PET
1st tumour in 25 pts
Insulinoma > non functioning > gastrinoma
Node +ve or metastases in 4 patients

Dalac et al. WorldMEN 2006
GEP in MEN 1 - Screening

How?

EUS Detection of PET in Asymptomatic Patients with Type 1 MEN

Wamsteker et al 2003

Prospective Evaluation of Imaging Procedures for the Detection of PET in Patients with MEN Type 1

Langer et al 2004

Prospective EUS evaluation of the Frequency of Non Functioning PDET in Patients with MEN Type 1

Thomas-Marques et al 2006
GEP in MEN 1 - Screening

Abnormal morphology

EUS
Resolution 1-2 mm
Good for pancreatic disease (80%)
Good for nodes (60%)
Less for gastrinoma – small duodenal tumours

SRS
<1cm tumours (30%)
Good for metastases
GEP in MEN 1 - Screening

Abnormal morphology

No Tumour identified
Repeat EUS at 3 years

Tumour/s identified
\( \leq 1 \text{ cm} \) repeat at 1 year
\( >1 \text{ cm} \) ?????
GEP in MEN 1 - Operation

Comparison of surgical results in patients with advanced and limited disease with MEN Type 1 and ZES

*Norton et al 2001*

The surgical management of MEN-1 pancreatoduodenal neuroendocrine disease.

*Hausman et al 2004*
Gastrin normal – duodenotomy not required
Intraoperative endoscopy
Intra operative USS
GEP in MEN 1 – Outcome

Management of Pancreatic Endocrine Tumours in MEN 1

Kouvaraki et al 2006

Is Surgery Beneficial for MEN 1 Patients With Small (<2 cm) Nonfunctioning PET?

Triponez et al 2006
GEP in MEN 1 – Outcome

Prognosis

Mean age at death is 51 years
80% of patients will live 10 years
Survival better in young/functioning/no distant metastases
Distant metastases are rare in the absence of liver metastases
♀   09/1974   Gene +ve MEN 1

@ 25 y   HPT surgery
@ 27 y   MRI pancreas - normal
@ 29 y   rising glucagon 55-83 (<50)
@ 30 y   MRI – mass in pancreatic tail

Distal pancreatectomy
Multifocal NET: 5 lesions showing ‘invasion’

Gut hormones normal
GTT normal

Don’t leave it too long
Glucagonoma
♀ 05/1964 Gene +ve Z-E syndrome

@ 22 y Prolactinoma surgery and DXT
@ 30 y HPT surgery
@ 40 y MRI lesion in pancreatic tail and 1.2 cm lesion in head of pancreas

Spleen preserving distal pancreatectomy
Pancreas: multifocal NET: 4 tumours 2-14mm diameter
Duodenum: 3 NET
Nodes: positive

BAO 3.1 mm H⁺/hr (<5)
GTT normal

Timing of surgery
‘Cure’ is possible
♂ 09/1984  Gene +ve MEN 1

@ 14 y  HPT surgery
@ 18 y  MRI – mass in tail of pancreas
        Gut hormones - normal
♂ 09/1984 Gene +ve MEN 1

@ 14 y HPT surgery
@ 18 y MRI – mass in tail of pancreas
Gut hormones - normal
Family History

@ 20 y Spleen preserving distal pancreatectomy
Pancreas: head – 9mm NET enucleated
body/tail - 3 lesions 7-19 mm
- micro tumours 1- 4 mm

@ 22 y GTT normal

Talk to the patient
Does age at onset influence surgical advice?
♂ 10/1957 Gene +ve Z-E syndrome

@ 39  4th operation for HPT

@40 MRI lesion in pancreatic tail
    lesion in head of pancreas

@49 Spleen preserving distal pancreatectomy
    Pancreas: multifocal NET:
    4 tumours 2-14mm diameter
    Duodenum: 3 NET.  Nodes

Multiple complications. Discharged 4 months post op
♀ 07/1948  Gene +ve  Z-E syndrome

@ 56 y  Abnormal MRI  2cm lesion in pancreatic head
1 cm lesion uncinate process

Spleen preserving distal pancreatectomy
Enucleation head and uncinate tumours
Excision gastric tumour and node metastases
Nil in duodenum

8 months post op – multiple hepatic metastases
Don’t leave it too late
Surgery for GEP in MEN 1

Screen early in gene positive individuals
Intervene if abnormal imaging and abnormal biochemistry
or
increasingly abnormal imaging
or
increasingly abnormal biochemistry
and
no metastases (excluding lymph nodes)

25% of patients will have liver metastases by the time they are symptomatic