

Write notes on **two** of the following:

1. Chromogranins
2. Gastrinoma (Zollinger-Ellison syndrome)
3. Carcinoid syndrome

1. Chromogranins

Highly conserved member of chromogranin/secretogranin family
Chromogranin A, B and C (CgC = Secretogranin 11)

Functions:

Largely unknown
Secretory granule formation
Precursor for other peptides
Paracrine growth effects
Antibacterial effects

Chromogranin A

49kDa, 439AA, monomeric, hydrophilic acidic glycoprotein

Widespread in endocrine and neuroendocrine tissue (Pituitary, parafollicular cells of thyroid, chief cells of parathyroid, islet cells, bronchi, GIT, skin). Not found in steroid hormone secreting cells.

Diagnostic: Non-specific neuroendocrine tumour marker (functioning and non-functioning tumours). Useful in the absence of specific markers (eg VIP, gastrin) for NET syndromes.

Prognostic: Concentrations correlate with tumour burden and malignancy

Monitoring: Concentrations falls with tumour debulking and somatostatin treatment

Increased in renal disease, liver disease and all causes of achlorrhya (including proton pump inhibitors)

May also be increased in other tumours – renal cell tumours etc

Special collection techniques.

“Pancreastatin”

Mid portion fragment of CgA 210-301
Raised in NETs with liver metastases
Concentrations proportional to tumour mass.

GAWK

Fragment of CgB (420-493)
Produced by a variety of endocrine tumours especially pancreatic endocrine tumours

2. Gastrinoma (Zollinger-Ellison syndrome)

Sites

Pancreatic (60%)

Duodenal (40%)

Clinical Features

Resistant multiple peptic ulceration: abdominal pain/ “dyspepsia”

Diarrhoea ± Steatorrhoea

Abdominal pain

Local effects

Associated with MEN 1

Incidence has fallen probably due to masking with Proton pump inhibitors

Diagnosis

Increased Gastric Acid output with (inappropriate) Hypergastrinaemia

Differential Diagnosis:

 Antral G Hyperplasia

 (Chronic renal failure

 Pyloric/parapyloric obstruction)

(Gastrin response to secretin)

Gastric acid response to pentagastrin.

Increased Chromogranin A

Other investigations

Serum Calcium – exclusion MEN 1

Imaging for localising tumour

Treatment:

Removal of tumour: but often small & multiple

Gastrectomy: Historical

Proton pump inhibitors

3. Carcinoid syndrome

Clinical Features (due to Humoral manifestations of carcinoid tumours);

Diarrhoea

Facial flushing

Bronchospasm

Pellagra:

Tumour metabolism of tryptophan to serotonin causes nicotinic acid deficiency

Right heart disease/failure:

Tricuspid regurgitation

Pulmonary regurgitation and stenosis

Right heart enlargement and dysfunction

Other Clinical Features

Local effects of primary and secondary tumours

Association with MEN 1

Manifestation of metastatic disease involving the liver

- Increased systemic concentrations of serotonin/ vasoactive peptides (histamine, kallikrein prostaglandins) because:
 - Portal vein serotonin/ vasoactive peptides escape hepatic degradation
 - Direct secretion of serotonin/ vasoactive peptides from liver metastases into the systemic circulation.
- Rarely carcinoid syndrome may occur in the absence of hepatic metastases with ovarian and bronchial carcinoid tumours which secrete serotonin/ vasoactive peptides directly into the systemic circulation
- Usually arise from Mid-gut carcinoid tumours

Diagnosis:

Raised 5HIAA: False +ve with drugs and diet
False -ve with drugs

Increased Chromogranin A (and B)

Other investigations

Usually known carcinoid: Imaging for extent for disease
CT and ultrasound; Somatostatin Receptor Scintigraphy

If first presentation:

Exclusion of MEN1

Imaging for primary;

Treatment

Usually Palliative

Control of symptoms: Somatostatin analogues

Reduce Tumour burden – debulking hepatic metastases with surgery or by hepatic artery embolisation.

Pellagra – Niacin

Heart Disease: Treat heart failure. Cardiac valvular surgery

Comments on answers to questions

Write notes on **two** of the following:

General comments

Most included irrelevant information in their answers.

Imaging (unless functional imaging) investigations are not usually diagnostic tests in hyper- or hypofunction.

1. Chromogranins

Few answered this question, but it was answered with correct emphasis on CgA as a NET marker. Little or no information on false positives

2. Gastrinoma (Zollinger-Ellison syndrome)

Most answering the question failed to mention increased gastric acid output (NB not necessarily the same as low gastric pH) with (inappropriate) hypergastrinaemia – the biochemical hallmark of ZES

3. Carcinoid syndrome

This was poorly answered. The question was about carcinoid syndrome whereas most candidates incorrectly interpreted the question “write all you know about carcinoid tumors”

Most candidates failed to mention that carcinoid syndrome is almost always a manifestation of metastatic carcinoid disease involving the liver.