J Triay, N Thorogood, D Wynick, KJ Bradley.
Department of Endocrinology, Bristol Royal Infirmary

Very Interesting Presentation: VIP Co-secretion by a Phaeochromocytoma

CASE HISTORY 62 year old lady

Medical history and presentation:

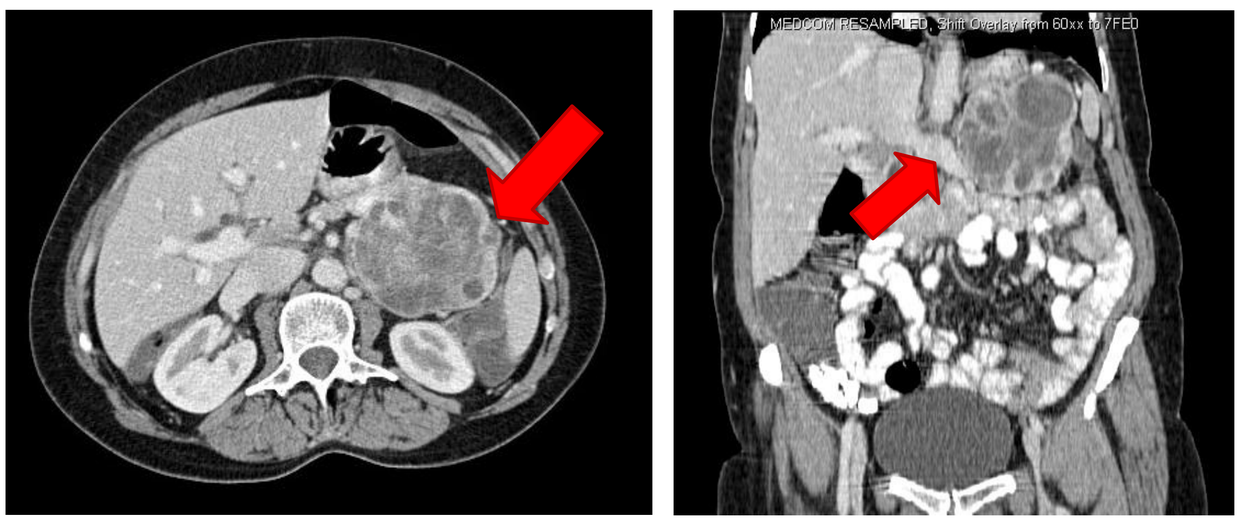
- 15 years ago – diagnosed with irritable bowel syndrome with alternating constipation and diarrhoea
- 5 years ago – diarrhoea became the dominant feature, bowel opening every 20 minutes daily
- Investigations negative for hyperthyroidism and coeliac disease but she was found to have a non-functioning anal sphincter
- 3 years ago - a colostomy was performed privately to improve her symptoms, but large volumes of stool continued to be passed daily. She had experienced episodes of palpitations and sweating, although these had resolved and appeared to coincide with menopause.
- August 2011, right upper quadrant abdominal pain leading to admission under the Hepatico-pancreatico-biliary surgeons . CT imaging was performed and subsequent referral made to Endocrinology.

Other Past Medical History: Hysterectomy for menorrhagia 2001, Pernicious anaemia

Drug History: Amitriptyline, Omeprazole, B12

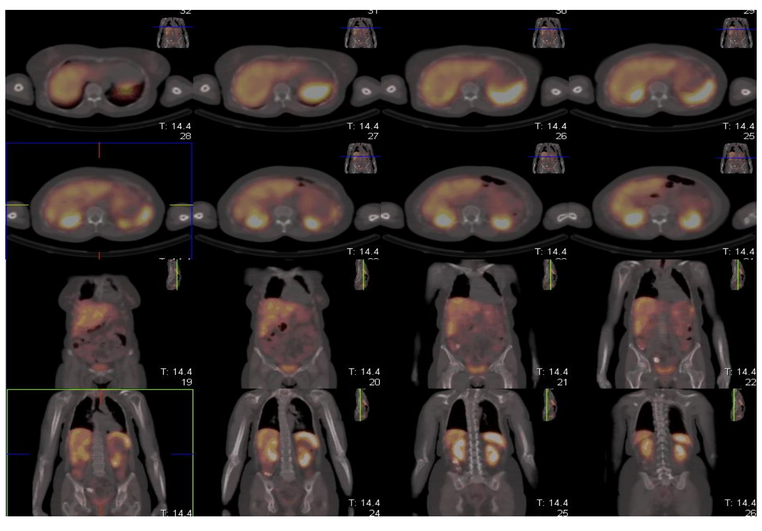
Examination: Normotensive, normal heart rate, no phenotype of Cushing's syndrome, no skin rashes

CT ABDOMEN



7cm multi-cystic tumour
Extending to the tail of the pancreas
Arising from the pancreas/left adrenal gland

OCTREOTIDE SCAN



Mildly avid uptake on MIBG

INVESTIGATIONS

Due to clinical suspicion plasma metanephrines were sent in addition to urinary catecholamines and demonstrated excess noradrenaline secretion.

CATECHOLAMINES			
Urinary Adrenaline	*37*	*nmol/24 Hrs*	*<100*
Urinary Noradrenaline	*694*	*nmol/24 Hrs*	*<800*
Dopamine	*12768*	*nmol/24 Hr*	*<3100*

METANEPHRINES			
Plasma Normetanephrine	*18562*	*pmol/L*	*120 - 1180*
Plasma Metanephrine	*18328*	*pmol/L*	*80 – 510*
Urinary Normetadrenaline	*11.2*	*Umol/24Hrs*	
Urinary Metadrenaline	*0.4*	*Umol/24Hrs*	

GUT HORMONES			
Vasoactive intestinal peptide	*100.0*	*pmol/L*	*<30.0*
Pancreatic polypeptide	*43*	*pmol/L*	*<300*
Gastrin	*24*	*pmol/l*	*<40*
Glucagon	*10.0*	*pmol/l*	*<50.0*
Somatostatin	*95*	*pmol/L*	*<150*
Chromogranin A	*35*	*pmol/L*	*<60*
Chromogranin B	*94*	*pmol/L*	*<150*

SURGICAL RESECTION

PRE-OPERATIVE MANAGEMENT

Appropriately alpha and beta blocked

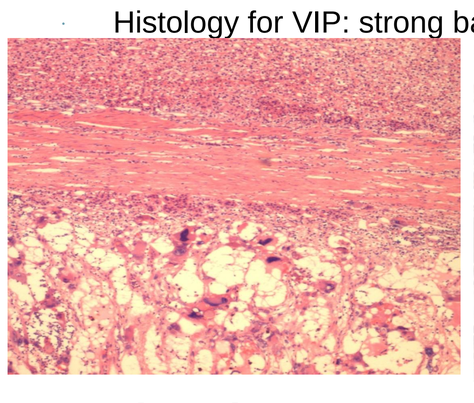
Admitted 3 days pre-operatively to optimize blood pressure and circulating volume.

Proceeded to left adrenalectomy

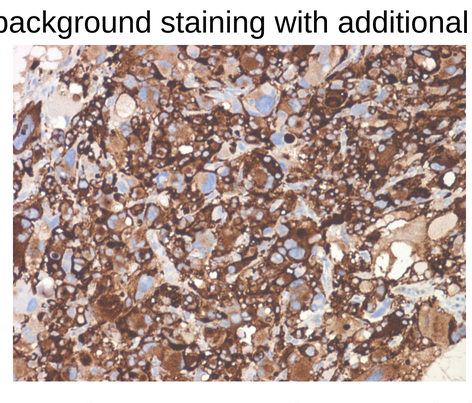
No hypoglycaemia; Haemodynamically stable peri- and post-operatively

HISTOLOGY: CONFIRMED PHAEOCHROMOCYTOMA

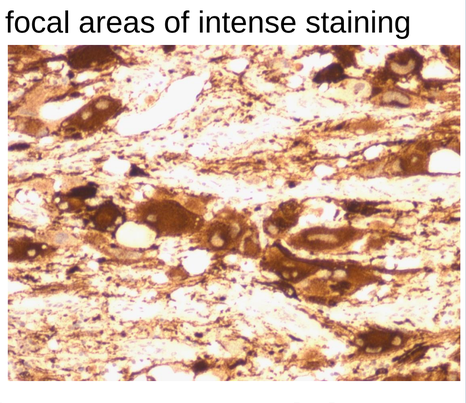
Histology for VIP: strong background staining with additional focal areas of intense staining



1. Adrenal tumour



2. Chromogranin A staining (Pale blue)



3. VIP staining (Brown)

POST-OPERATIVE COURSE

Stoma output reduction to normal volumes (bag emptying once daily)

PLASMA METANEPHRINES			
Plasma Normetanephrine	*532*	*pmol/L*	*120 - 1180*
Plasma Metanephrine	*101*	*pmol/L*	*80 - 510*

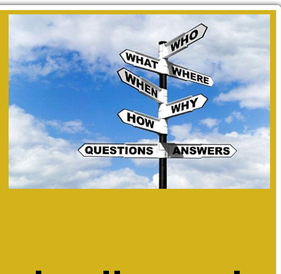
GUT HORMONES			
Vasoactive intestinal peptide	*6.0*	*pmol/L*	*<30.0*
Pancreatic polypeptide	*29*	*pmol/L*	*<300*
Gastrin	*19*	*pmol/l*	*<40*
Glucagon	*38.0*	*pmol/l*	*<50.0*
Somatostatin	*29*	*pmol/L*	*<150*
Chromogranin A	*35*	*pmol/L*	*<60*
Chromogranin B	*45*	*pmol/L*	*<150*

Final diagnosis: VIP secreting Phaeochromocytoma

VIP SECRETING PHAEOCHROMOCYTOMA

- Rare but documented association
- Seemingly invariably associated with elevated dopamine
- 20 case reports in literature (975-2012).
- Notably, hypertension is rarely recorded, possibly due to vasodilatory/dehydrating effects of VIP

Points considered for further management



1. What is the appropriate long-term endocrine follow-up?
2. Should genetic screening be recommended?
3. Are plasma metanephrines the baseline screen of choice in all or only in selected patients?
4. Can we pursue stoma reversal for our patient?

References
Smith SL, Slappy AL, et al. Pheochromocytoma producing vasoactive intestinal peptide. Mayo Clin Proc. 2002 Jan;77(1):97-100.
Quarles Van Ufford-Mannesse P, et al. A patient with neurofibromatosis type 1 and watery diarrhoea syndrome due to a VIP-producing adrenal phaeochromocytoma. J Intern Med. 1999 Aug;246(2):231-4.
Fisher BM, MacPhee GJ, et al. A case of watery diarrhoea syndrome due to an adrenal phaeochromocytoma secreting vasoactive intestinal polypeptide with coincidental autoimmune thyroid disease. Acta Endocrinol (Copenh). 1987 Mar;114(3):340-4.
Sackel SG, Manson JE, et al. Watery diarrhea syndrome due to an adrenal pheochromocytoma secreting vasoactive intestinal polypeptide. Dig Dis Sci. 1985 Dec;30(12):1201-7.
Trump DL, Livingston JN, Baylin SB. Watery diarrhea syndrome in an adult with ganglioneuroma-pheochromocytoma: identification of vasoactive intestinal peptide, calcitonin, and catecholamines and assessment of their biologic activity. Cancer. 1977 Oct;40(4):1526-32.