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Beckwith-Wiedemann Syndrome and Bilateral Phaeochromocytoma: a Diagnostic Challenge

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Background

Beckwith-Wiedemann Syndrome (BWS) is a rare overgrowth disorder secondary to mutations in growth-regulatory genes on chromosome 11p15.5. A well-established association exists between BWS and benign and malignant tumours, most commonly Wilms' tumour and hepatoblastoma.[1] We describe a patient with BWS and bilateral phaeochromocytoma/paraganglioma (PPGL), which is much less well described.

Initial presentation

- A 14 year-old girl with genetically confirmed BWS presented with headaches, sweating, palpitations and hypertension (BP 177/117).
- Previously routine screening had detected a bladder rhabdomyoma (aged 2 years) and a pancreatoblastoma (aged 7 years), both surgically resected.
- Biochemistry was in keeping with a diagnosis of phaeochromocytoma (Table 1) and an abdominal MRI demonstrated bilateral complex adrenal cysts ≤ 2cm (Figure 1), however Iodine-123-meta-iodobenzylguanidine (MIBG)-scan showed no abnormal sites of activity.

Test	Result	Normal range
24 hr-urine catecholamines 456ml urine (incomplete sample)	Normetadrenaline 1.6 umol Metadrenaline 0.1 umol	0.6-3.5 0.2-1.4
24 hr-urine catecholamines 2L urine	Normetadrenaline **22.3** umol Metadrenaline 0.8 umol	0.6-3.5 0.2-1.4
Plasma catecholamines	Normetadrenaline **9514** pmol/L Metadrenaline 295 pmol/L	120-1180 80-510

Table 1. Biochemistry results

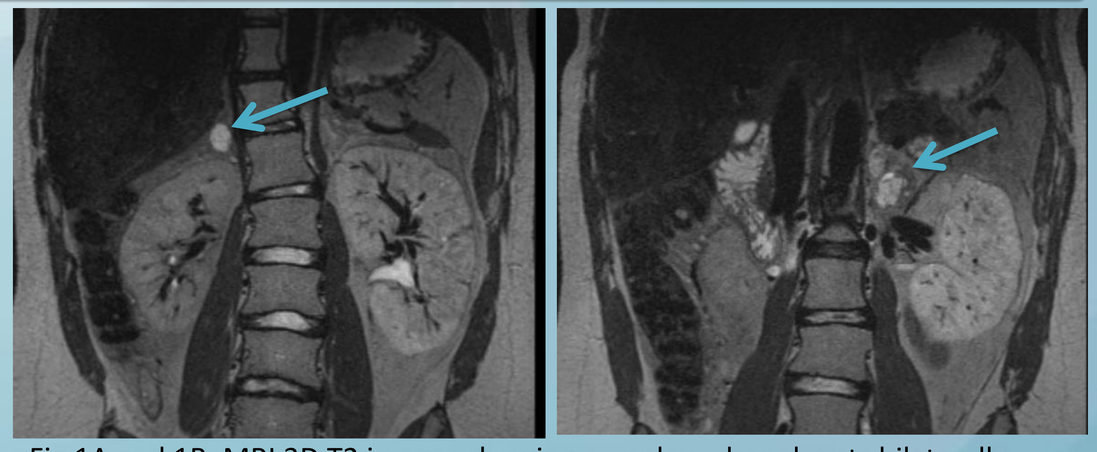


Fig 1A and 1B. MRI 3D T2 images showing complex adrenal cysts bilaterally

- Due to a strong clinical suspicion of phaeochromocytoma a fat-suppressed fludeoxyglucose (FDG)-PET scan was undertaken (Figure 2).
- Abnormal uptake was seen within both adrenal glands, suggesting bilateral phaeochromocytoma.
- No additional genetic mutations more commonly associated with phaeochromocytoma (MEN, SDH-A/B/C/D, NF-1) were discovered.

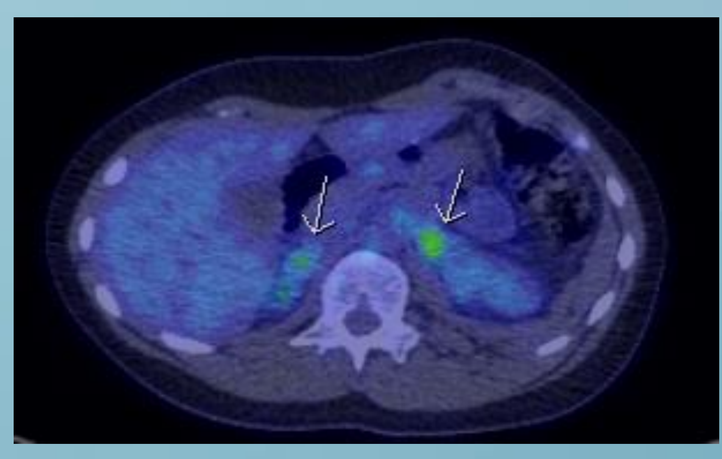


Fig 2. Fat-suppressed FDG-PET scan showing abnormal uptake within both adrenal glands

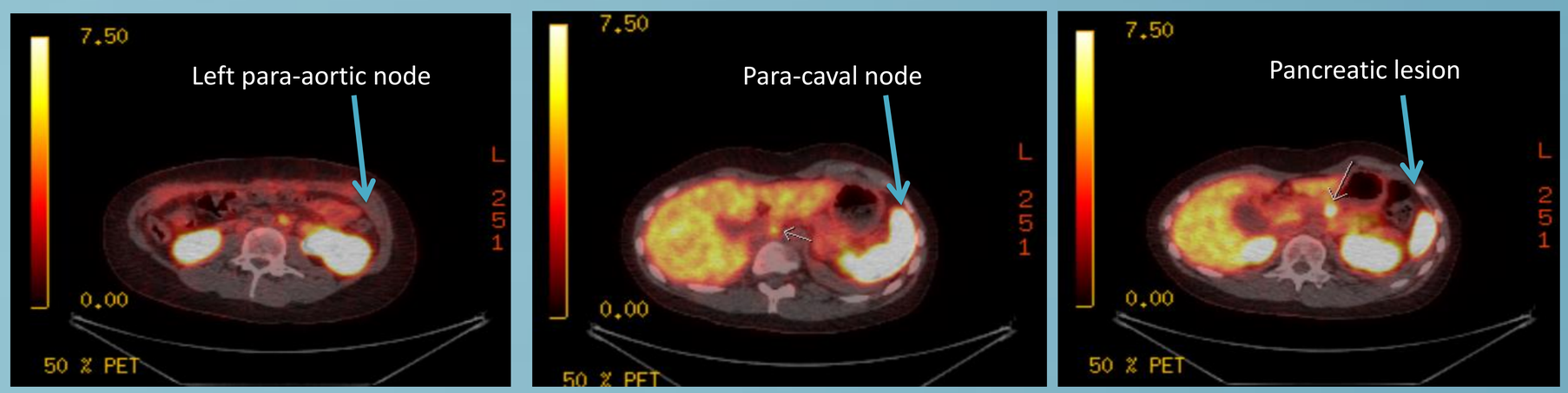
Management

- A personalised management plan was created using the BSPED endorsed Paediatric Endocrine Tumours consensus[2] and the adult Phaeochromocytoma and Paraganglioma guideline[3]
- She was commenced on the alpha-blocker Doxazocin 1mg once daily as an outpatient, then admitted for BP optimisation using phenoxybenzamine. This dose was gradually increased under close monitoring until complete alpha-blockade was achieved.
- Large volumes of intravenous fluids were necessary pre-operatively for volume expansion.
- Following successful bilateral adrenalectomies, histological analysis confirmed phaeochromocytoma.

Post-operative course

- Hydrocortisone was initially commenced intravenously intra-operatively, then converted to oral hydrocortisone (10 mg morning, 5 mg at lunchtime, 5 mg evening) and fludrocortisone 100mcg once daily once tolerated.
- Despite successful bilateral adrenalectomies she remained hypertensive (systolic BP >130) and further investigation found plasma normetanephrine remained elevated (4152pmol/L).
- A Gallium-68 DOTANOC PET-CT scan showed increased uptake in para-caval and left para-aortic lymph nodes and in the pancreas (Figure 3).

Fig 3a,b,c. Gallium-68 DOTANOC PET-CT scan showing areas increased uptake as indicated



- Further surgical resection was undertaken and histology confirmed extra-axial PGLs and the presence of neuroendocrine tissue in the pancreatic lesion.
- Gallium uptake in the lymph nodes and pancreatic lesion indicates somatostatin receptors are present therefore Lutathera (Lutetium-177 DOTA-Octreotide) radionuclide therapy may be a treatment option.
- Currently the patient remains stable on adrenal replacement (Hydrocortisone 10 mg morning, 5 mg lunchtime, 5 mg evening) and Fludrocortisone 150 mcg once daily and blood pressure is well-controlled (BP 101/66) on Doxazocin 2mg once daily.

Learning points:

- This case demonstrates the importance of on-going vigilance for tumour development in patients with BWS.
- Phaeochromocytomas not detected on MIBG-scanning are more likely to be metastatic and due to SDHB mutations, which carry an unfavorable prognosis [4]. This case highlights the importance of undertaking further imaging after a negative MIBG scan if the clinical and biochemical picture is highly suggestive of phaeochromocytoma.
- An updated guideline on the management of paediatric PPGLs is needed.

References
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There are no conflicts of interest to declare

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