High prevalence of germinal mutations in pheochromocytomas with normal urinary metanephrines results

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Introduction

Pheochromocytomas are tumors derived from the adrenal-medullary chromaffin cells that normally produce catecholamines. Rarely these tumors are non-secreting. In the assessment of a suspected pheochromocytoma, guidelines recommend dosing urinary or plasma metanephrines.

Objective

To evaluate the prevalence of pheochromocytomas biochemically non-secreting and their differences

Methods

We searched all patients with measurements of metanephrines made in an endocrinology department since 1999 (when Clinical Pathology was computerized). We included all those who had performed adrenalectomy in this institution with pheochromocytoma histology. Urinary metanephrines were measured with spectrophotometric chromatographic method (Pisano).

Results

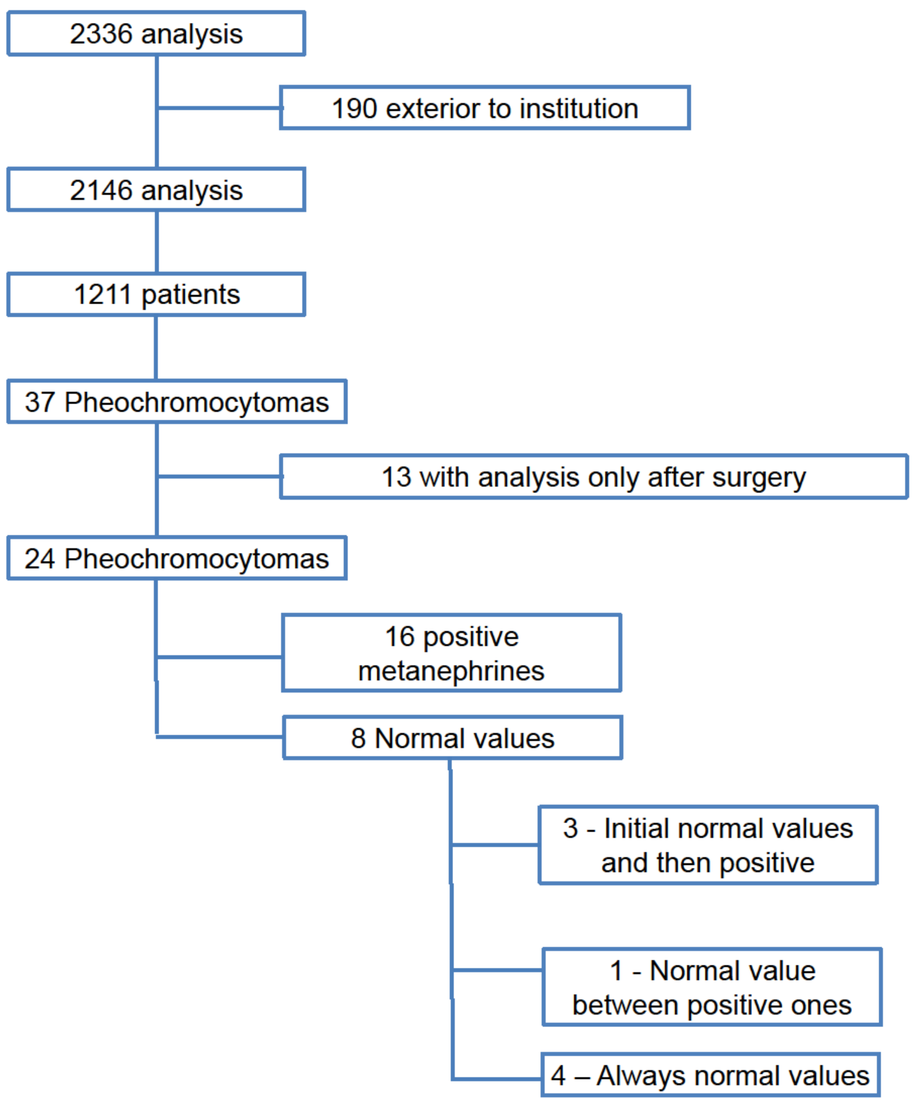

Figure 1. Work-up flow

3 – Analysis initial normal and then positive

CASE 1:

F 31a
MEN2a

Jan 1999	18/02	27/02	18/03	21/03
Met (<1)	0,7	0,2	0,8	**1,3**
AVM (<14)	9	5,2	9,7	8,4
MRI: **Right adrenal nodule with 3cm**				

CASE 2:

M 35
MEN2a

2010	11/2012	01/2013
Met: 0,5	0,9	**1,1**
MRI: sem alt	**MRI: Left adrenal nodule with 9mm**	

CASE 3:

F 27
MEN2a

10/2008	11/2009
Met: 0,5	**1,4**
RMN: **Right adrenal nodule with 10mm**	**MRI: nodule with 30mm**

1 – Normal value between positives

CASE 4:

67 years, with **always with positive metanephrines with a right adrenal tumor with 2,6cm.**

Begins **metiltirosine e fenoxibenzamine** for surgery . Has **normal metanephrine** under medication.

4 – Always normal values

	Age	Sex	Medical history	Image	Met	Genetics
Case 5	24	F	MEN2a Surgery for right pheoctomocytoma in 2009	CT: Left adrenal tumor with 15mm	**0,8**	MEN2a
Case 6	26	F	--------	CT: Left adrenal tumor with 124x100mm	**0,4**	SDHC
Case 7	59	F	--------	MRI: Right adrenal tumor with 30mm	**0,9**	SDHB
Case 8	48	M	--------	MRI: Right adrenal tumor with 32mm	**0,6**	SDHB

Discussion/Conclusion

In literature its described that pheocromocytomas can have normal metanephrines if they are small tumors (< 1 cm) in asymptomatic patients, tumors where noradrenaline and adrenaline are not synthesized or metabolized, tumors predominantly or exclusively producers of dopamine[1] . Our study describes Pheochromocytomas that can have normal metanephrine values when have diameters less than 1.5cm , when there is use of drugs that interfere with metanephrine's production and when they have mutations that may interfere with catecholamine production (including SDHB). Tmmers 2008 discovered that SDHB mutations can lead to tirosine hidroxilase absence which leads to a deficit catecolamine production. Our study reveals the need for repeat measurements of urinary metanephrines for exclusion of pheochromocytoma when there is an image of a tumor in an adrenal gland. It also revealed a high prevalence of germline mutations in biochemically silent pheochromocytomas

A van Berkel, J W M Lenders and H J L M Timmers, Biochemical diagnosis of phaeochromocytoma, and paraganglioma, European Journal of Endocrinology (2014) 170, R109–R119
Timmers, H. **Biochemically Silent Abdominal Paragangliomas in Patients with Mutations in the *Succinate Dehydrogenase Subunit B* Gene**J Clin Endocrinol Metab. December 2008, 93(12):4826–4832

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