

Supplementary data from:

Adrenal venous sampling (AVS) in Primary Bilateral Macronodular Adrenocortical Hyperplasia (PBMAH): A study of 16 patients

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Table 1: Clinical, biochemical and radiological characteristics. Abbreviations: CS: Cushing's syndrome; MACS: Mild autonomous Cortisol secretion; F: Female; M: Male; LDDST: Low Dose Dexamethasone Suppression Test; UFC: 24h urinary free cortisol measurement; LNSLC: late-night salivary cortisol; ACTH: Adrenocorticotrophic hormone; WxDxH: Width x Depth x Height; Wt: Wildtype; NA: not available.

Table 2: Biochemical results from AVS. Lower limits of quantification: Cortisol 2 µg/dl, Aldosterone: 35 ng/ml, Metanephrine: 36 pg/ml, Normetanephrine: 48 pg/ml, DHEA-S 0.1µg/ml, Androstenedione 0.24 ng/ml. When the concentrations of the measured hormones were below the lower limit of detection of the assay, half of the lower limit of detection was used for calculation.

Abbreviations: SI: Selectivity index; LI: Lateralization index; L: Left; R: Right.

Table 3: Biochemical and genetic assays at the study sites Würzburg and Graz. Abbreviations: PFBHA: 0-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine hydrochloride; MSTFA: methyltrimethylsilyltrifluoroacetamide; PCR: polymerase chain reaction.

Table 1

Patient No.	Sex and Age (at diagnosis)	Clinical presentation	LDDST [$\mu\text{g/dl}$]	UFC [$\mu\text{g}/24\text{h}$]	LNSLC [ng/ml]	ACTH [pg/ml]	Adrenal size on imaging				ARMC5 Status
							Left		Right		
							WxDxH [cm]	Volume [ml]	WxDxH [cm]	Volume [ml]	
Patient 1	F 58	Overt CS	7.6	410	7.9	2.5	2.8x5.1x4.2	60	5.5x4.9x5.1	137.4	wt
Patient 2	F 60	Overt CS	5.6	169	2.3	9	2.6x5x4.2	54.6	2.3x4.3x5.6	55.4	wt
Patient 3	F 56	Overt CS	15.1	207	NA	<5	5x4.8x5.8	139.2	3.5x3.9x4.5	61.4	wt
Patient 4	M 48	Overt CS	33.7	847	10.3	3	8.2x10.5x9.9	852.4	4.7x3.9x6.3	115.5	MUT c.2290C>T, p.R764X
Patient 5	F 58	Overt CS	4.1	222	3.3	<2	2.2x3.4x4	29.9	3.7x4.8x5.3	94.1	wt
Patient 6	F 38	Overt CS	14.5	324	5.9	3	4x1.3x4.4	22.9	1.4x3.5x4.9	24	wt
Patient 7	F 72	Overt CS	3.1	322	0.7	4	3x2.3x4.1	28.3	1.8x2.1x2.5	9.5	NA
Patient 8	F 50	Overt CS	13.2	NA	5.3	2	2.6x3.3x1.9	16.3	1.5x3.5x3.7	19.4	MUT NM_001105 247:exon3:c.

											G646A:p.V216M
Patient 9	F 64	MACS	5.6	59	0.7	NA	3.2x2.8x3.7	33.2	2.4x2.6x3.9	24.3	NA
Patient 10	F 56	Overt CS	8.0	104	4.1	4	2.7x2.9x2.8	21.9	3.5x3.8x3.1	41.2	wt
Patient 11	F 58	Overt CS	4.3	151	5.6	<2	2.2x3.1		3.1x2.0		MUT NM_001105 247:exon1:c. 237_238insC :p.A80Rfs*23
Patient 12	F 60	Overt CS	25.1	232	4.32	3	3.8x2x1.5	11.4	5.6x2.5x4.6	64.4	NA
Patient 13	F 55	MACS	5.5	21.3	3.6	<5	3.8x4.7x3.4	60.7	2.0x2.3x3.1	14.3	MUT c.41T>A = p.Phe14Tyr, rs151069962
Patient 14	F 77	Overt CS	8.8	36.8	1.6	6.3	3.3x2.6x3.0	25.7	2.8x1.9x2.7	14.4	MUT c.508A>G = p.Ile170Val, rs35923277
Patient 15	F 69	Overt CS	17.2	58	30.0	<5	4.5x2.6x2.2	25.7	5.4x2.6x3.1	43.5	wt

Patient 16	F 62	Overt CS	17.4	50	4.1	<5	2.0x2.2		2.8x1.9		MUT c.1961 G>T, p.Arg654Leu and c.1864+73C> T
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Table 2

	Perip heral	Left adrenal	Right adrenal	SI Left	SI Right	LI L/R ratio	LI R/L ratio
Patient 1							
Cortisol [µg/dl]	6.4	28.1	27.6	4.4	4.3	1.0	
Aldosterone [ng/l]	78.7	342.3	241.8	4.3	3.1		1.4
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							
DHEA-S [µg/ml]	2.6	2.9	3.1	1.1	1.2	1.1	
Androstenedione [ng/ml]							
Patient 2							
Cortisol [µg/dl]	15.1	106	35.8	7.0	2.4	3.0	
Aldosterone [ng/l]							
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							
DHEA-S [µg/ml]	<0.1	<0.1	0.2	1	4	11.8	
Androstenedione [ng/ml]							
Patient 3							
Cortisol [µg/dl]	16.8	44.3	32.8	2.6	2.0	1.4	
Aldosterone [ng/l]	<35	58.2	83.2	3.3	4.8	1.9	
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							
DHEA-S [µg/ml]							
Androstenedione [ng/ml]							
Patient 4							
Cortisol [µg/dl]	22.9	127.2	125.7	5.6	5.5	1.0	
Aldosterone [ng/l]	<35	110	116	6.3	6.6	1.1	
Metanephrine [pg/ml]	<36	87	365	5.4	22.8	4.2	
Normetanephrine [pg/ml]	<48	52	100	2.2	4.2	1.9	
DHEA-S [µg/ml]							
Androstenedione [ng/ml]							
Patient 5							
Cortisol [µg/dl]	12.9	37.7	271.9	2.9	21.1		7.2
Aldosterone [ng/l]	<35	1720	272	98.3	15.5		45.6
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							
DHEA-S [µg/ml]							
Androstenedione [ng/ml]							
Patient 6							
Cortisol [µg/dl]	10.8	512	616.8	47.4	57.1		1.2
Aldosterone [ng/l]							
Metanephrine [pg/ml]	<36	5987	2288	332.6	127.1		3.2
Normetanephrine [pg/ml]	66	1617	568	24.5	8.6		3.4
DHEA-S [µg/ml]							
Androstenedione [ng/ml]							

Patient 7							
Cortisol [$\mu\text{g/dl}$]	8.6	38.9	216.9	4.5	25.2		5.6
Aldosterone [ng/l]							
Metanephrine [pg/ml]	40	88	2105	2.2	52.6	4.3	
Normetanephrine [pg/ml]	<48	<48	552	1.0	23	4.1	
DHEA-S [$\mu\text{g/ml}$]							
Androstenedione [ng/ml]							
Patient 8							
Cortisol [$\mu\text{g/dl}$]	10.4	633.5	50.9	60.9	4.9	12.5	
Aldosterone [pg/ml]	239	1840	2190	7.7	9.2	14.8	
Metanephrine [pg/ml]	<36	2096	1005	116.4	55.8	6	
Normetanephrine [pg/ml]	<48	601	371	25	15.5	7.7	
DHEA-S [$\mu\text{g/ml}$]							
Androstenedione [ng/ml]							
Patient 9							
Cortisol [$\mu\text{g/dl}$]	7.8	179	17	22.9	2.2	10.5	
Aldosterone [ng/l]	<35	179	220	10.2	12.6	12.9	
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							
DHEA-S [$\mu\text{g/ml}$]							
Androstenedione [ng/ml]							
Patient 10							
Cortisol [$\mu\text{g/dl}$]	11.7	41.3	271.7	3.5	23.2		6.6
Aldosterone [pg/ml]	86	140	357	1.6	4.2		2.6
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							
DHEA-S [$\mu\text{g/ml}$]							
Androstenedione [ng/ml]	<0.24	9.4	24.24	78.3	202		2.6
Patient 11							
Cortisol [$\mu\text{g/dl}$]	14.5	154.8	32.4	10.7	2.2	4.8	
Aldosterone [pg/ml]	94	1270	329	13.5	3.5	1.2	
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							
DHEA-S [$\mu\text{g/ml}$]							
Androstenedione [ng/ml]	0.66	7.94	7.25	12.0	11.0	4.4	
Patient 12							
Cortisol [$\mu\text{g/dl}$]	9.0	23.7	39.7	2.6	4.4		1.7
Aldosterone [pg/ml]	52	239	277	4.6	5.3		1.4
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							
DHEA-S [$\mu\text{g/ml}$]							
Androstenedione [ng/ml]							
Patient 13							
Cortisol [$\mu\text{g/dl}$]	10.6	35.6	22.0	3.4	2.1	1.6	
Aldosterone [ng/l]	37	63	315	1.7	8.5	8.1	
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							

DHEA-S [$\mu\text{g/ml}$]							
Androstenedione [ng/ml]							
Patient 14							
Cortisol [$\mu\text{g/dl}$]	12.4	74.3	46.9	6.0	3.8	1.6	
Aldosterone [ng/l]	37	1415	420	38.2	11.4		2.1
Metanephrine [pg/ml]							
Normetanephrine [pg/ml]							
DHEA-S [$\mu\text{g/ml}$]							
Androstenedione [ng/ml]							
Patient 15							
Cortisol [$\mu\text{g/dl}$]	8.5	28.8	56.5	3.4	6.6		2.0
Aldosterone [ng/l]	47	1008	>1320	21.4	28.1		1.5
Metanephrine [pg/ml]	<28	2410	1770	86.1	63.2		2.7
Normetanephrine [pg/ml]	57	663	503	11.6	8.8		2.6
DHEA-S [$\mu\text{g/ml}$]	0.18	0.23	0.24	1.3	1.3		1.9
Androstenedione [ng/ml]							
Patient 16							
Cortisol [$\mu\text{g/dl}$]	16.6	48.8	>75	2.9	4.5		1.5
Aldosterone [ng/l]	<37	311	667	8.4	18.0	1.4	
Metanephrine [pg/ml]	995	47	47	0.0	0.0		1.5
Normetanephrine [pg/ml]	210	68	40	0.3	0.2		2.6
DHEA-S [$\mu\text{g/ml}$]	0.04	0.06	0.11	1.5	2.8	1.2	
Androstenedione [ng/ml]							

Table 3

Assay	Würzburg, Germany	Graz, Austria
Cortisol in serum	Immulite 2000 XPi chemiluminescent immunometric assay (Siemens Healthcare Diagnostics Inc.)	ADVIA Centaur Cortisol-test on a CENTAUR XP (Siemens Healthcare Diagnostics Inc.)
ACTH	Immulite 2000 XPi chemiluminescent immunometric assay (Siemens Healthcare Diagnostics Inc.)	Immulite 2000 XPi chemiluminescent immunometric assay (Siemens Healthcare Diagnostics Inc.)
24h urinary free cortisol	Cortisol radioimmunoassay kit (Beckman Coulter)	LC-MS/MS on a HP5-MS column (derivatisation with PFBHA (0-(2,3,4,5,6-pentafluorobenzyl) hydroxylamine hydrochloride) and MSTFA (methyltrimethylsilyltrifluoroacetamide)
Cortisol in saliva	Lumineszenz immunoassay (IBL International GmbH)	Enzyme-linked immunosorbent assay kit (Demeditec Diagnostics)

Aldosterone	Automated chemiluminescence immunoassay (CLIA, iSYS, Immuno Diagnostic Systems)	Chemiluminescence assay (IDS-iSYS Aldosterone assay; Immunodiagnostic Systems Ltd.)
Metanephrine	2-MET Plasma Fast track radioimmunoassay (Labor Diagnostika Nord)	MetCombi Plasma Enzyme-linked immunosorbent assay (DRG Instruments GmbH)
Normetanephrine	2-MET Plasma Fast track radioimmunoassay (Labor Diagnostika Nord)	MetCombi Plasma Enzyme-linked immunosorbent assay (DRG Instruments GmbH)
DHEA-S	Immulite 2000 XPi chemiluminescent immunometric assay (Siemens Healthcare Diagnostics Inc.)	Enzyme-linked immunosorbent assay (Labor Diagnostika Nord)
Androstendione	Immulite 2000 XPi chemiluminescent immunometric assay (Siemens Healthcare Diagnostics Inc.)	Enzyme-linked immunosorbent assay (Siemens Healthcare Diagnostics Products Ltd.)
ARMC5 mutation status		PCR for Sanger Sequencing