

SUPPLEMENTARY DATA

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Supplementary Table S1: Clinical features of the 109 patients with Cowden syndrome all carrying PTEN mutation

Case	Age	Sex	PTEN Genotype/ PTEN Mutation	Brain MRI Findings	Breast	Thyroid	Renal Cancer	Endometrium	Colorectal Cancer	Brain Tumor	Reference
1	60	M	c.395G>A p.(Gly132Asp)	Mn		b	Y			Y	[1]
2	54	F	c.388C>T p.(Arg130Ter)	Mn	50,52m b	b		b		Y	[1]
3	23	M	c.382A>G p.(Lys128Glu)	CH		b				N	[1]
4	45	F	c.697C>T p.(Arg233Ter)	LD	44m b	42m b				Y	[1]
5	44	F	c.734_737del4		b	41m b		38m		N	[1]
6	36	F	c.865_871delAAAGTAG	V	b	36m b				N	[1]
7	50	M	c.253+1G>A	LD		44m b				Y	[1]
8	51	F	Exon 2 deletion		44m b	b				N	[1]
9	29	F	c.394GG>TT p.(Gly132Phe)	Mn	b	b		29m		Y	PS
10	26	F	c.335T>C p.(Leu112Pro)	MnLD	b	b		b		Y	[2]
11	75	F	c.202T>C p.(Tyr68His)		b	b				N	[2]
12		M	c.386G>A p.(Gly129Glu)	GB	b					Y	[3]
13			c.386G>A p.(Gly129Glu)			b				N	[3]
14	43	M	c.469G>T p.(Glu157Ter)	LD Mn						Y	[4]
15	57	M	c.368A>G p.(His123Arg)			b				N	[5]
16	42	F	c.370T>C p.(Cys124Arg)			b				N	[5]
17	38	F	c.387C>T p.(Arg130Ter)		b	b				N	[5]
18	35	F	c.15delC		35m	b				N	[6]
19	28	M	p.(His123Gln)			b			Y	N	[7]
20	39	M	c.634+5G>A			b			Y	N	[7]
21	50	M	Y	Mn		b				Y	[8]
22	38	M	Y	LD		b				Y	[8]
23	34	M	Y	V		b				N	[8]
24	56	M	Y	V		b				N	[8]
25	58	F	Y	LD V	b			m		Y	[8]
26	36	F	Y		m					N	[8]

(Continued)

Case	Age	Sex	PTEN Genotype/ PTEN Mutation	Brain MRI Findings	Breast	Thyroid	Renal Cancer	Endometrium	Colorectal Cancer	Brain Tumor	Reference
27	26	F	Y		m	m				N	[8]
28	72	M	Y							N	[8]
29	36	F	Y		m			b		N	[8]
30	50	F	Y		m			m		N	[8]
31	48	M	Y			m			Y	N	[8]
32	48	F	Y		m b					N	[8]
33	32	F	Y							N	[8]
34	41	F	c.389G>A p.(Arg130Gln)		29m b	b		b		N	[1]
35	30	F	c.287C>G p.(Pro96Arg)		b	b				N	[1]
36	44	F	c.634+1G>C		43m b	b	44Y			N	[1]
37	58	F	c.697C>T p.(Arg233Ter)		56m b	b		53m	34Y	N	[1]
38	58	F	c.1033C>G p.(Leu345Val)		46m b	b		41m b		N	[1]
39	46	F	c.401T>C p.(Met134Thr)		43m b	46m b		b		N	[1]
40	58	F	Whole gene deletion		56m b	b		b		N	[1]
41	25	F	c.253+1G>C		b	b				N	[1]
42	57	M	c.253+1G>C			b				N	[1]
43	26	F	c.486_487delCA		b	b				N	[1]
44		F	p.(Gly165Glu)		b	m b				N	[9]
45	31	F	c.1003C>T p.(Arg335Ter)	MS	21m	10m				N	[10]
46	54	F	c.1003C>T p.(Arg335Ter)		48m	42b				N	[10]
47	47	F	c.106G>A p.(Gly36Arg)		28,31m	b		b		N	[11]
48	43	F	c.388C>T p.(Arg130Ter)		b	b				N	[11]
49	51	M	c.375insTTTA			b				N	[11]
50	50	F	c.115G>C p.(Arg39Pro)		m b	b		b		N	[12]
51	41	M	c.697C>T p.(Arg233Ter)	Mn		b				Y	[13]
52	70	F	c.589A>T p.(Lys197Ter)			b				N	[13]

(Continued)

Case	Age	Sex	PTEN Genotype/ PTEN Mutation	Brain MRI Findings	Breast	Thyroid	Renal Cancer	Endometrium	Colorectal Cancer	Brain Tumor	Reference
53	39	M	c.219-222delAAAGA			b				N	[13]
54	48	F	c.1004G>T p.(Arg335Leu)		m	b				N	[14]
55	38	F	c.632insG			b				N	[14]
56	40	M	I3+1delGT							N	[14]
57	62	F	I3+1delGTAA		m	m				N	[14]
58	28	M	c.697C>T p.(Arg233Ter)		b	b				N	[14]
59	38	F	p.(Asn48Lys)		m	b		m		N	[15]
60	43	F	c.48-48insA		b	m		b		N	[16]
61		F	p.(Tyr68Asp)							N	[17]
62	31	M	c.209T>C p.(Leu70Pro)			m				N	[18]
63	75	F	p.(Tyr68His)		b	b				N	[19]
64		F	p.(Arg130Leu)		m b	m b			Y	N	[19]
65		F	p.(Gly165Val)	Mn	b	b				Y	[19]
66	57	F	c.1003C>T p.(Arg335Ter)		43,51m					N	[20]
67	55	F	c.388C>T p.(Arg130Ter)		48m	18b		37m b	Y	N	[20]
68	30	F	c.406T>C p.(Cys136Arg)		19b	18b			Y	N	[20]
69	38	M	c.701G>A p.(Arg234Gln) ?	OD Mn						Y	[21]
70	56	F	c.530-531delAT		53m	b				N	[22]
71	49	M	c.247insT							N	[22]
72	46	M	c.277C>T p.(His93Tyr)			b				N	[22]
73	72	M	p.(Pro96Gln)			b				N	[23]
74	62	F	c.528T>G p.(Tyr176Ter)		m	b				N	[23]
75	53	F	p.(His123Asp)			b				N	[23]
76	32	F	p.(Arg335Ter)	LD	b	b				Y	[23]
77	45	F	p.(Gln214Ter)		m b	m				N	[23]
78	38	F	c.487-491delA		b					N	[23]
79	36	M	p.(Arg233Ter)			b				N	[23]
80			c.388C>T p.(Arg130Ter)							N	[24]
81	35	M	c.389G>A p.(Arg130Gln)			b				N	[25]

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Case	Age	Sex	PTEN Genotype/ PTEN Mutation	Brain MRI Findings	Breast	Thyroid	Renal Cancer	Endometrium	Colorectal Cancer	Brain Tumor	Reference
82	54	F	I9-1A>G	LD	b	b				Y	[26]
83	56	F	c.388C>T p.(Arg130Ter)		m	b			Y	N	[27]
84	25	F	c.359T>G Stopp codon	LD		b				Y	[28]
85	27	F	c.395G>A p.(Gly132Ter)	LD		b				Y	[28]
86	46	F	c.68T>A p.(Leu22Ter)		46m					N	[29]
87	24	F	c.68T>A p.(Leu22Ter)		24m	18m				N	[29]
88	34	F	c.328C>T p.(Gln109Ter)		34m					N	[29]
89	31	F	c.565A>T p.(Arg188Ter)	NF	31m	b				Y	[29]
90	29	F	c.565A>T p.(Arg188Ter)		29b					N	[29]
91	27	F	c.697C>T p.(Arg232Ter)		27m					N	[29]
92	42	F	c.1003C>T p.(Arg334Ter)		41b	42b		42m	42Y	N	[29]
93	50	F	c.1028T>A p.(Val332Glu) +c.1039T>C p.(Phe346Leu)	NE	50m	49b				Y	[29]
94	48	F	c.1028T>A p.(Val332Glu) +c.1039T>C p.(Phe346Leu)		30b	32b		48m		N	[29]
95	42	F	c.1028T>A p.(Val332Glu) +c.1039T>C p.(Phe346Leu)		33b	33b		42m		N	[29]
96		M	c.1028T>A p.(Val332Glu) +c.1039T>C p.(Phe346Leu)	PN						Y	[29]
97	42	F	c.1028T>A p.(Val332Glu) +c.1039T>C p.(Phe346Leu)		42m					N	[29]
98	43	F	exons 6-9del		m b	b		b		N	[30]
99	56	M	c.534T>G p.(Tyr178Ter)			m				N	[31]
100	54	F	c.334C>G p.(Leu112_Lys164del)		m b					N	[31]
101	37	M	c.388C>TSNP c.1026+32T>G p.(Arg130Ter)			b			Y	N	[31]
102	53	M	c.395G>A p.(Gly132Asp)			b	Y			N	[31]
103	53	M	c.80-?_164+?del			b				N	[31]
104	44	F	c.49C>T p.(Gln17Ter)		b	b				N	[31]
105	38	M	c.634+2T>C							N	[31]

(Continued)

Case	Age	Sex	PTEN Genotype/ PTEN Mutation	Brain MRI Findings	Breast	Thyroid	Renal Cancer	Endometrium	Colorectal Cancer	Brain Tumor	Reference
106	48	F	c.389G>A p.(Arg130Gln)		m b			b		N	[31]
107	37	M	c.376G>C p.(Ala126Pro)			b				N	[31]
108	50	F	c.464A>G p.(Tyr155Cys)		m	b				N	[32]
109	48	F	p.(Gln214Ter)	Me	30m	44b	Y			Y	[33]

Abbreviations used: (b) benign; (C) Cystic lesion; (CH) Chiari I Malformation; (F) female; (GB) Glioblastoma; (LD) Dysplastic gangliocytoma; (m) malignant; (M) male; (Me) Metastases; (Mn) Meningioma; (MS) Multiple sclerosis; (NE) Malignant neuroma; (N) absent; (NF) Neurofibroma; (OD) Oligodendroglioma; (PN) Pineal-gland tumor; (PS) present study; (V) Venous anomaly/angioma; (Y) present.