Acquired partial lipodystrophy is associated with increased risk for developing metabolic abnormalities

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Objective

Acquired partial lipodystrophy (APL) is a rare disorder characterized by progressive selective fat loss. In previous studies, metabolic abnormalities were reported to be relatively rare in APL, whilst they were quite common in other types of lipodystrophy syndromes. However, there has been no systematic study on metabolic abnormalities in APL so far.

Methods

We systematically evaluated 21 Turkish patients with APL who were enrolled in a prospective follow-up protocol. Subjects were investigated for metabolic abnormalities. Fat distribution was assessed by whole body MRI. Hepatic steatosis was evaluated by ultrasound, MRI and MR spectroscopy. Patients with diabetes underwent a mix meal stimulated C-peptide/insulin test to investigate pancreatic beta cell functions. Leptin and adiponectin levels were measured.

Results

Fifteen individuals (71.4%) had at least one metabolic abnormality. Six patients (28.6%) had diabetes, 12 (57.1%) hypertrigylceridemia, 10 (47.6%) low HDL cholesterol, and 11 (52.4%) hepatic steatosis. Steatohepatitis was further confirmed in 2 patients with liver biopsy. Anti-GAD was negative in all APL patients with diabetes. APL patients had lower leptin and adiponectin levels compared to patients with type 2 diabetes and healthy controls. However, contrary to what we observed in patients with congenital generalized lipodystrophy (CGL), we did not detect consistently very low leptin levels in APL patients. The mix meal test suggested that APL patients with diabetes had a significant amount of functional pancreatic beta cells, and their diabetes was apparently associated with insulin resistance.

Table-1: Clinical and laboratory characteristics of patients with APL.

Patient No	Actual Age (years)	Gender (M/F)	The age when APL was first diagnosed (years)	The age when fat loss was first noticed (years)	Follow-up (months)	Current treatment	Auto-antibody positivity	Low C3	Fasting glucose (mg/dL) N: 70-100	Triglyceride (mg/dL) N: 40 -150	Total cholesterol (mg/dL) N: 80-240	LDL (mg/dL) N: 30-160	HDL (mg/dL) N: > 40 men > 50 women	Insulin (µIU/mL) N: 0.4-8.1	HOMA-IR N: 0.8-2.3
1	14	M	11	11	39	Metformin, ramipril	+	+	127	322	163	100	23	15.31	4.8
2	34	F	29	13	57	Lispro, glargine, EPO, calcium, calcitriol	-	+	141	354	149	49	29	20.79	7.24
3	45	F	35	7	120	None	-	-	83	213	181	95	43	3.03	.62
4	52	F	50	44	23	None	-	-	85	220	237	149	44	20.40	4.28
5	60	F	58	48	21	None	+	-	91	81	216	134	66	5.66	1.27
6	26	M	22	11	48	Metformin, pioglitazone, repaglinide, glargine, gemfibrozil	+	-	134	215*	179	96	40	24.23	7.98
7	15	M	9	7	72	None	+	+	92	123	154	93	36	4.87	1.11
8	45	F	45	30	6	None	-	-	94	149	178	118	50	13.54	3.14
9	46	M	44	13	19	Aspart, detemir, fenofibrate	-	-	182	210*	215	126	47	32.85	14.76
10	26	M	25	7	11	Metformin, pioglitazone	-	+	114	184	156	91	28	8.14	2.29
11	17	M	10	8	84	None	-	+	84	94	172	101	52	1.68	.35
12	18	M	10	8	96	None	-	+	90	80	175	122	46	11.10	2.47
13	48	M	47	17	10	None	+	-	84	82	205	136	53	3.42	.71
14	30	F	29	16	14	None	-	+	97	159	211	128	59	10.73	2.57
15	12	F	9	7	45	None	-	-	99	182	207	108	62	8.07	1.97
16	34	M	33	20	13	Gemfibrozil, fish oil	-	-	92	4084*	384	129	12	5.21	1.18
17	45	F	44	14	10	None	-	-	82	79	176	116	44	NA	NA
18	15	F	14	14	12	None	-	+	89	84	180	110	60	3.88	.85
19	9	M	7	5	24	None	-	+	82	62	154	92	68	4.10	.83
20	22	M	22	17	3	None	-	-	80	162	140	70	38	3.31	0.65
21	34	F	29	20	60	Aspart, glargine, metformin, fenofibrate, ramipril	+	+	171	836*	153	42	21	24.25	10.24

Table-2: Comparison of APL patients with- and without diabetes, subjects with CGL, type 2 diabetes and healthy controls.

	Age (years)	Gender (M/F)	Fasting glucose (mg/dL) N: 70-100	HbA1c (%) N: 4.5-5.7	Triglyceride (mg/dL) N: 40 -150	Total cholesterol (mg/dL) N: 80-240	LDL (mg/dL) N: 30-160	HDL (mg/dL) N: 20 -55 men 20-45 women	Insulin (µIU/mL) N: 0.4-8.1	HOMA-IR N: 0.8-2.3
APL with diabetes (n = 6)	30 (23-37)	4/2	138 †* (124-174)	7.2 (6.18-8.88)	269 †‡* (204-475)	160 (152-188)	94 (47-107)	29 †‡ (23-42)	22.51†* (13.52-26.4)	8.74 †‡* (5.62-16.54)
APL without diabetes (n = 15)	30 (15-45)	7/8	89 * (83-92)	NA	123 * (81-182)	180 (172-211)	116 (95-129)	50 (43-60)	5.04 * (3.39-10.82)	1.15 * (0.69-2.49)
CGL (n = 8)	27.5 (20-30)	3/5	100.5 (97-152.5)	7.7 (6.3-10.2)	558 (181-1371)	170 (134-359)	90 (67-106)	29 (27-46)	16.72 (16.02-25.91)	5.79 (3.75-10.93)
Type 2 diabetes (n = 15)	33 (31-34)	8/7	131 (122-163)	7 (6.7-8.2)	153 ‡ (90-203)	224 (176-256)	144 (106-178)	48 ‡ (41-62)	9.08 (7.98-13.73)	2.99 ‡ (2.58-5.28)
Healthy controls (n = 16)	32 (29-34)	8/8	85 † (80-88)	NA	91† (75-116)	188 (174-202)	124 (105-140)	49 † (40-59)	3.95 † (3-5.39)	0.84 † (0.6-1.07)

NA: Not applicable. †$p < 0.05$ for APL with diabetes vs. healthy controls, ‡$p < 0.05$ for APL with diabetes vs. type 2 diabetes, *$p < 0.05$ for APL with diabetes vs. APL without diabetes.

Table-3: Characteristics of subjects evaluated by the mix meal test.

	Age (years)	Gender (M/F)	Duration of diabetes (years)	Fasting glucose (mg/dL) N: 70-100	HbA1c (%) N: 4.5-5.7	Triglyceride (mg/dL) N: 40 -150	Total cholesterol (mg/dL) N: 80-240	LDL (mg/dL) N: 30-160	HDL (mg/dL) N: 20 -55 men 20-45 women	Insulin (µIU/mL) N: 0.4-8.1	HOMA-IR N: 0.8-2.3
APL with diabetes (n = 5)	26 (20-40)	4/1	3 (2-14)	134 † (121-177)	8.1 (6.15-9.45)	215 †* (197-579)	163 (155-197)	96 (67-113)	28 (22-44)	24.23 † (11.73-28.55)	10.24 † (5.35-18.32)
Type 1 diabetes (n = 5)	26 (21-37)	4/1	3 (1.5-6.5)	133 ‡ (117-182)	8.1 (6.4-8.6)	77 * (65-125)	189 (162-199)	120 (89-134)	53 (43-59)	NA	NA
Type 2 diabetes (n = 5)	29 (28.5-31.5)	4/1	3 (1.5-4.5)	141 ‡ (125-162)	8 (6.6-8.15)	147 (76-172)	223 (163-237)	135 (103-161)	46 (36-59)	12.44 ‡ (8.67-16.88)	5.28 ‡ (2.68-6.05)
Healthy controls (n = 5)	29 (29-32)	4/1	NA	85 †*‡ (79-87)	NA	103 † (72-121)	195 (185-227)	134 (122-146)	44 (41-62)	4.65 †‡ (3.17-6.18)	0.92 †‡ (0.65-1.31)

Patient-2 was excluded because of ESRD which may cause falsely elevated insulin and C-peptide levels. NA: Not applicable. †$p < 0.05$ for APL with diabetes vs. healthy controls, ‡$p < 0.05$ type 1 diabetes vs. healthy controls, §$p < 0.05$ type 2 diabetes vs. healthy controls, *$p < 0.05$ for APL with diabetes vs. type 1 diabetes.

Conclusions

APL is associated with increased risk for developing metabolic abnormalities.

Close long-term follow-up is required to identify and manage metabolic abnormalities in APL.

Figure-1: The clinical features of APL patients who developed diabetes during follow-up.
1a: Female control. MR images show normal fat distribution in a 28 year-old healthy woman (Height: 167 cm, weight: 58 kg, BMI: 20.8 kg/m², waist: 70 cm, hip: 94 cm, waist to hip ratio: 0.75). **1b:** Male control. MR images show normal fat distribution in a 26 year-old healthy man (Height: 182 cm, weight: 78 kg, BMI: 23.5 kg/m², waist: 83 cm, hip: 105 cm, waist to hip ratio: 0.79). **1c:** Patient-1. Coronal WB TSE T1 weighted image reveals fat loss in the head and neck, upper trunk and upper extremities (I). Axial TSE T1 weighted image shows fat loss on the upper trunk and upper extremities (II). In axial plane, in and out of phase GRE T1 weighted images (III and IV) show diffuse signal loss on out of phase image that is in consistent with hepatosteatosis. Hydrogen-1 MR spectroscopic image (V) shows a significant peak of hepatic triacylglycerol (arrows) near water peak (dot). **1d:** Patient-2. Coronal WB TSE T1 weighted image shows fat loss in the head and neck, upper extremities and the upper trunk, sparing the lower extremities (I). Axial TSE T1 weighted image demonstrates the lack of fat on the upper trunk and upper extremities (II). Eye examination shows Drusen maculopathy (III). **1e:** Patient-6. Coronal WB TSE T1 weighted image demonstrates the fat loss (I). Axial TSE T1 weighted image shows the subcutaneous fat loss on the upper trunk and upper extremities (II). In axial plane, GRE T1 weighted images show diffuse signal loss on out of phase image (III and IV). Hydrogen-1 MR spectroscopic image (V) shows a significant peak of hepatic triacylglycerol (arrows) near water peak (dot). **1f:** Patient-9. Coronal WB TSE T1 weighted image shows the altered fat distribution (I). Axial TSE T1 weighted image demonstrates the fat loss on the upper trunk and upper extremities (II). In axial plane, GRE T1 weighted images (III and IV) show diffuse signal loss on out of phase images in consistent with hepatosteatosis. Hydrogen-1 MR spectroscopic image (V) shows a significant peak of hepatic triacylglycerol (arrows) near water peak (dot). **1g:** Patient-10. Coronal WB TSE T1 and axial TSE T1 weighted images demonstrate fat loss (I and II). In axial plane, in and out of phase GRE T1 weighted images (III and IV) show hepatic fat content. Hydrogen-1 MR spectroscopic image (III) shows a slight peak of hepatic triacylglycerol (arrows) near water peak (dot). **1h:** Patient-21. Coronal WB TSE T1 and axial TSE T1 weighted images demonstrate the loss of fat (I and II). Adipose tissue in the gluteal region and lower extremities are preserved (I). In axial plane, GRE T1 weighted images (III and IV) show diffuse signal loss on out of phase images. Hydrogen-1 MR spectroscopic image (V) shows a significant peak of hepatic triacylglycerol (arrows) near water peak (dot).

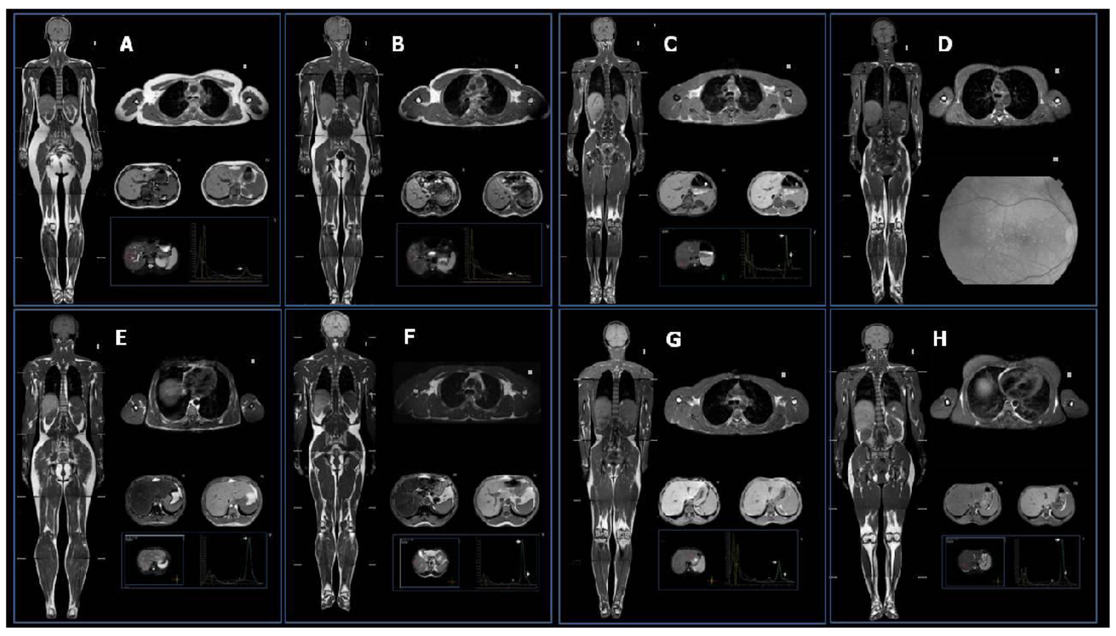


Figure-2: Fasting leptin (2a) and adiponectin (2b) levels in APL patients with diabetes.

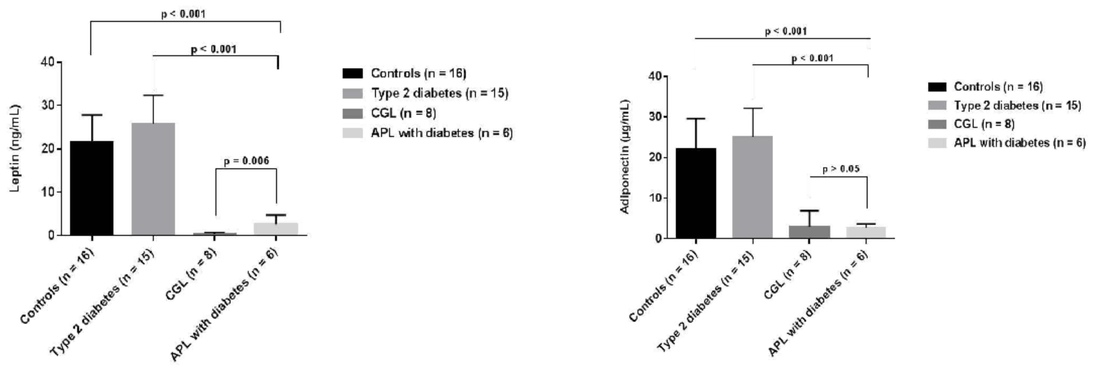
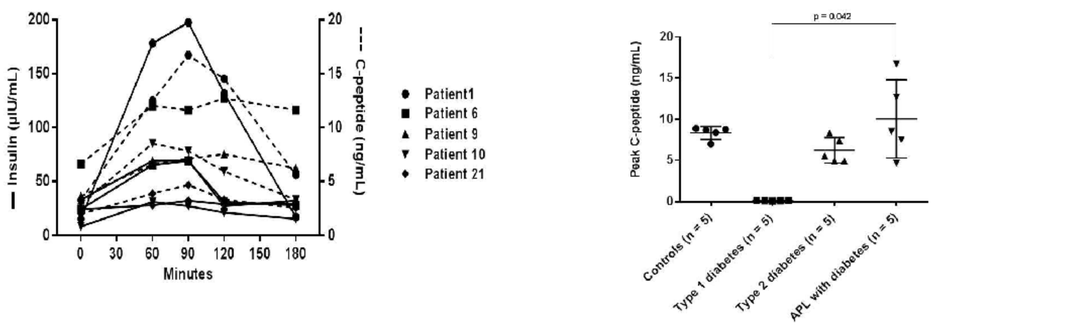


Figure-3: Basal and mix meal stimulated C-peptide and insulin levels in APL patients with diabetes (3a). Peak C-peptide levels (3b).



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