A case of autoimmune polyglandular syndrome type I presenting as progressive generalized lipodystrophy in a 15-month-old child.

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Background: Autoimmune polyglandular syndrome type 1 (APS1) is a monogenic autoimmune disease caused by defects in autoimmune regulator gene (*AIRE*). The classic clinical triad is composed of Addison disease, hypoparathyroidism, and chronic mucocutaneous candidiasis, however other endocrine and non-endocrine features of APS1 may occur. Lipodystrophies (LDs) are heterogeneous disorders characterized by selective loss of body fat. Acquired LDs are known to be associated with autoimmune diseases, like systemic lupus erythematosus, juvenile dermatomyositis, glomerulonephritis and APS type II (1,2), but to our knowledge it was never considered as a possible manifestation of APS1. Here we report on a challenging diagnosis of APS1 presenting in a 15-month-old boy with progressive generalized lipodystrophy.

Objective. To describe an unusual clinical manifestation of APS1.

Methods. Congenital lipodystrophy candidate genes (*ZMPSTE24, LMNA, BSCL2, PLIN1, PTRF, LMNB2, POLD1, AKT2, CIDEC, PIK3CA, PPARG, PSMB8, CAV1, PPP1R3A, AGPAT2)* were sequenced using a custom Ion Ampliseq panel and PGM semiconductor sequencer (Ion Torrent). p.R257X mutation in *AIRE* gene was analysed by real-time PCR.

Case description: A boy from a non-consanguineous family presented at the age of 15 months with progressive weight loss and subcutaneous fat disappearance, most evident on the limbs. Sequencing of congenital lipodystrophy candidate genes showed no mutations. During his fourth year of life autoimmune hepatitis (with rapid progression to hepatic cirrhosis Child-Pugh class C) and oral candidiasis were diagnosed consequently. Immunosuppressive therapy with prednisone normalized liver function, and the dose was reduced to 10 mg/day. After a year of steroid therapy there were still evident signs of lipodystrophy: absence of subcutaneous fat on the limbs and in gluteal area (skin folds less than 5 mm and 10 mm, respectively), prominent subcutaneous veins (Fig.1), undetectable leptin level, hyperinsulinemia (Tab.1). At the age of 4.5 years the patient presented with symptoms of adrenal crisis, hyponatremia, his renin was >500 mcIU/ml, ACTH > 300 pg/ml. Adrenal insufficiency was diagnosed and fludrocortisone 0.05 mg/day and 5 mg of hydrocortisone in the evening was administered in addition to previous therapy. APS1 was suspected, which was confirmed by detecting a homozygous p.R257X mutation in *AIRE* gene.

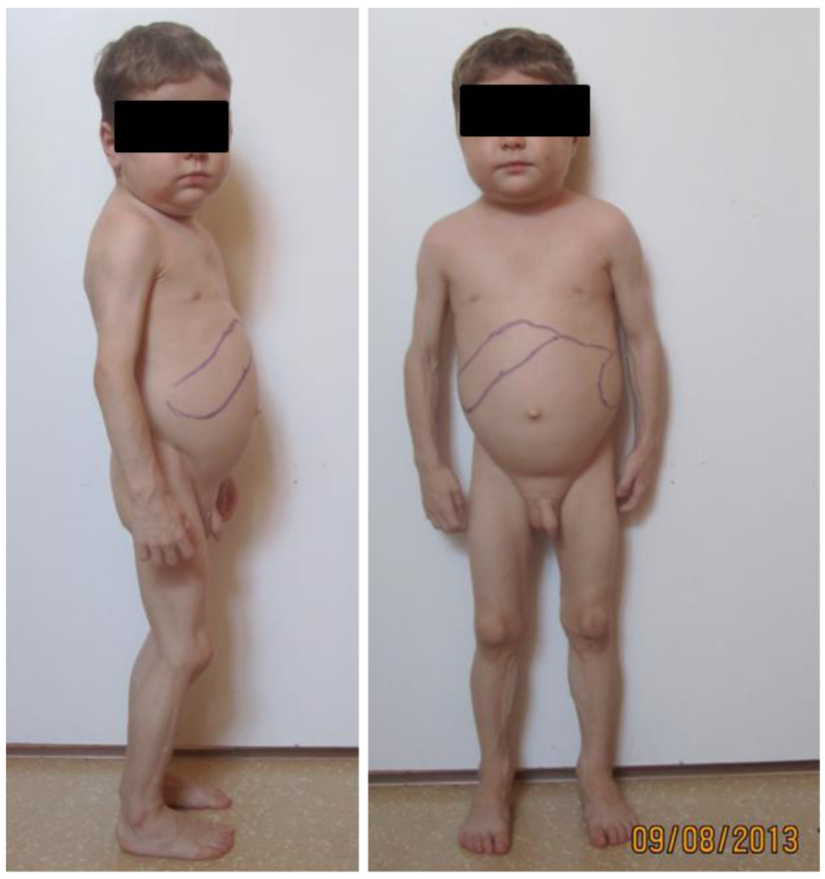

Fig.1

Laboratory data			
Fasting blood glucose (mmol/L)	3.8-4.6	Leptin, ng/ml	<1
Hemoglobin A1c (%)	5.8	Insulin, mcU/ml (1.9-23)	40-60
AST (IU/L)	28-600	Renin, mcIU/ml (4.4 – 46.1)	>500
ALT (IU/L)	36-900	ACTH, pg/ml (0-46)	> 300
Sodium levels, mmol/l (134-145)	122-131	PTH, pg/ml (10-66)	12
Calcium, mmol/L (2.2-2.7)	2.5		

Table 1

Conclusion

Acquired generalized lipodystrophy is known to be associated with autoimmune disorders. To our knowledge, however, this is the first time generalized lipodystrophy has been described as an initial manifestation of APS1.

[1]Chan JL, Oral EA. Clinical classification and treatment of congenital and acquired lipodystrophy. Endocr Pract. 2010; 16:310–323Owen CJ, Cheetham TD. Diagnosis and management of polyendocrinopathy syndromes. Endocrinol Metab Clin North Am. 2009; 38(2): 419-36
[2]Misra A, Garg A. Clinical features and metabolic derangements in acquired generalized lipodystrophy: case reports and review of the literature. Medicine (Baltimore). 2003 Mar;82(2):129-46.

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