EARLY-ONSET AUTOINFLAMMATORY PARTIAL LIPODYSTROPHY CHARACTERIZED BY RECURRENT FEVER AND RASH: CANDLE SYNDROME

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Disclosure statement: The authors have nothing to disclose.

Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature

* A recently described autoinflammatory disease that manifests in early infancy

* Recurrent fever, violaceous swelling of the eyelids, purpuric skin lesions, hypochromic anemia and elevated acute phase reactants.

* Autosomal recessively inherited and associated with partial lipodystrophy, growth retardation and hepatomegaly.

* *PSMB8* (proteasome subunit β type 8) mutation was identified in majority of the cases.

14-year-old girl

Complaint: Short stature, rash, recurrent fever and finger swelling, hepatosplenomegaly and cytopenia since 2-3 months of age.

Past history: Born to non-consanguineous parents from the same village after an uneventful term pregnancy. A history of growth hormone therapy for 2 years without sufficient response.

Physical examination: Normal mental motor development, severe growth retardation, lipodystrophy of face and limbs, hepatosplenomegaly, minimal joint contractures in the fingers, pubic hair and breast development consistent with Tanner stage II (Figure 1).

Figure 1. Lack of fat tissue in the face, asymmetrical gluteal fat, growth chart (red dots indicate GH treatment)

Laboratory: Hypochromic microcytic anemia (Hb 8,9g/dl, MCV 60,5), hypertriglyceridemia (TG 239mg/dl), elevated ferritin levels (Ferritin 539,6ng/ml). No insulin resistance (Glukoz 86mg/dl, insulin 8,85uU/ml, HOMA-IR 1,89).

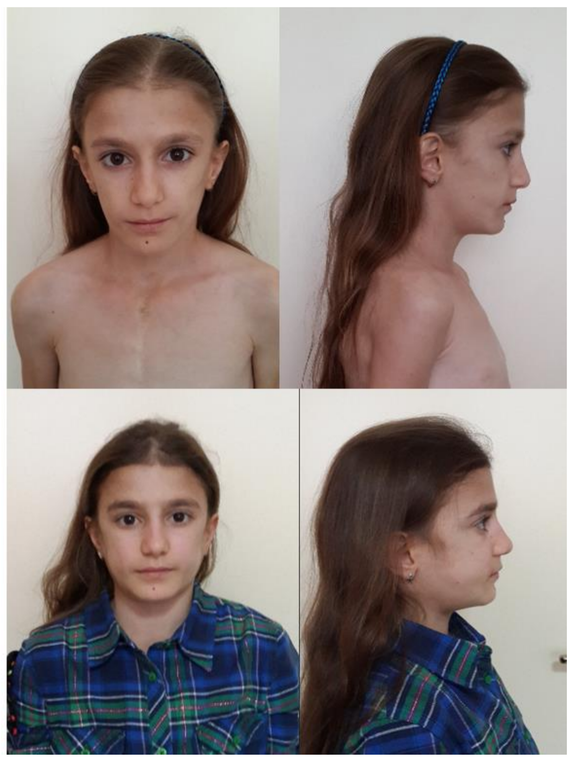
Whole body MRI : Asymmetric thinning and signal changes of fat tissue.

Karyotype: 46,XX

Skin biopsy: Panniculitis with neutrophilic infiltration

Genetic analyses: *PSMB8* mutation and whole exome sequencing was negative.

Treatment



*High-carbohydrate, low-fat diet

*Methylprednisolone treatment resulted in cessation of episodes of fever and rash.

*Anakinra 100 mg/d s.c. (IL-1 receptor antagonist) was not enough to lower inflammatory markers.

Figure 2. Appearance before and after treatment

Discussion

Lipodystrophy is characterized by regional or total loss or absence of subcutaneous fat. This can occur either in the presence or absence of metabolic abnormalities, and with diverse clinical presentations.

Among recently described lipodystrophy syndromes, autoinflammatory group include JMP (Joint contractures, Muscle atrophy, microcytic anemia and Panniculitis-induced childhood-onset lipodystrophy) and CANDLE syndromes which were reported in <100 cases so far.

PSMB8 mutations, recently reported to cause JMP syndrome, were established as cause of CANDLE syndrome as well.

Because dysregulation of the IFN signaling pathway was identified, IFN pathway may be a target for treatment in these patients.

Conclusion

*Lipodystrophy syndromes are included in the differential diagnosis of the patients admitted with early diabetes, severe hypertrigliseridemia, hepatosteatosis, HSM, acanthosis nigricans and PCOS.

*Patients with growth retardation, skin rashes and signs of inflammation should be searched for lipodystrophy as well, and CANDLE syndrome should be kept in mind.

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