

EP332: A Novel Clinical Phenotype of Acquired Partial Lipodystrophy Associated with Intensive Childhood Cytostatic Treatment

Introduction

- Lipodystrophy is a rare clinical syndrome characterized by subcutaneous fat loss, metabolic syndrome and fat maldistribution¹
- Common causes are HIV therapy, specific genetic mutations and autoimmune disease¹
- Partial lipodystrophy of the limbs with severe insulin resistance has been reported²

➤ **AIM: To report on a novel phenotype of partial acquired lipodystrophy with severe insulin resistance and elevated leptin levels, associated with intensive cytotoxic treatment in childhood**

Methods

- Detailed description of two cases with this specific phenotype
- Both patients were referred for treatment refractory type 2 diabetes

- Both had received intensive cytotoxic treatment in childhood
- Genetic and auto-immune testing was negative, and no underlying endocrine disorder was identified (i.e. Cushing's syndrome, lipid metabolism disorders)
- Treatment with pioglitazone was initiated

Patient 1: Case history

- 43 year old Caucasian female
- Treated with intensive polychemotherapy for leukemic lymphosarcoma at age 6 through 13
- Presented with treatment resistant diabetes, hypertension and dyslipidemia
- Complaints: central fat deposition, high glucose levels
- Current therapy: atorvastatine, tolbutamide, lantus in increasing dose
- Physical: BP 170/100 mmHg, bmi 23 kg/m²; Notable excess fat deposition at face, trunk, upper arms. Lipoatrophy of hips and distal extremities



Patient 2: Case history

- 22 year old Caucasian female
- Treated with high dose cyclophosphamide and total body irradiation for aplastic anemia at age 12
- Presented with treatment resistant diabetes, hypertriglyceridemia
- Complaints: recurrent graft-versus-host of the skin. High glucose levels despite metformin. Central fat deposition
- Current therapy: metformin, s.c. insulin in increasing dose
- Physical: BP 160/90 mmHg, bmi 22 kg/m² Severe fibrous skin scarring due to GvHD, notable lipoatrophy of extremities and hips, excess fat deposition at the trunk



Patient 1: Relevant laboratory results

	Before pioglitazone	After pioglitazone	Reference values
ALAT	42	26	< 34 U/L
Gamma GT	118	51	< 38 U/L
Triglycerides	1.8*	=	< 2.30 mmol/L
HbA1c	66	36	< 42 mmol/mol Hb
Fasting glucose	9.3	5.1	3.1 – 6.0 mmol/L
C-peptide	4.1	2.1	0.3 – 1.3 nmol/L
Leptin	35.1	55.3	3.7 – 11.1 µg/L

*While taking high dose statin therapy

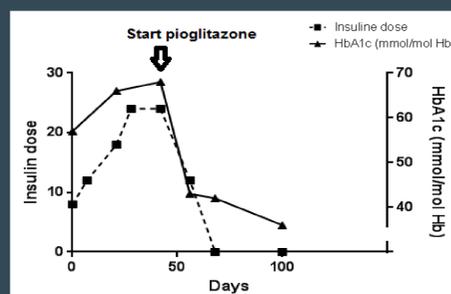
Patient 2: Relevant laboratory results

	Before pioglitazone	After pioglitazone	Reference values
ALAT	74	47	< 34 U/L
Gamma GT	222	70	< 38 U/L
Triglycerides	29.9	6.8	< 2.30 mmol/L
HbA1c	52*	34*	< 42 mmol/mol Hb
Fasting glucose	10.9	4.6	3.1 – 6.0 mmol/L
C-peptide	2.0	ND	0.3 – 1.3 nmol/L
Leptin	15.5	ND	3.7 – 11.1 µg/L

*Falsely low due to high red blood cell turn over. Fructosamine was 407 µmol/L (ref: 0 – 285) before treatment

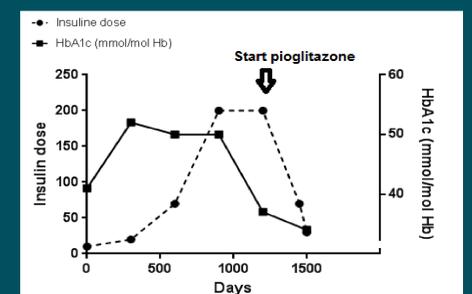
Patient 1: Clinical course

After initiation of pioglitazone 30mg once daily, blood pressure, glucose metabolism and liver enzymes normalized. No change in fat maldistribution



Patient 2: Clinical course

After careful initiation of pioglitazone 30mg once daily, insulin requirement decreased dramatically. Also, blood pressure, liver enzymes and triglycerides improved. No change in fat maldistribution



Conclusions

- Acquired partial lipodystrophy can be associated with intensive cytostatic treatment in childhood.
- This phenotype, characterized by loss of subcutaneous fat at the extremities and buttocks in the presence of elevated leptin levels, did not match previously reported types of lipodystrophy.
- Pioglitazone treatment appears to be particularly effective at treating the specific associated metabolic disorders.



References

- Garg A.. J Clin Endocrinol Metab 2011
- Strickland LR et al. Diabetes Care 2013

Acknowledgments

We would like to thank the patients for their permission to present their clinical case histories

Contact

m.f.nijhoff@lumc.nl

