

Prospective Follow-up of HIV-Infected Children and Young People with Lipodystrophy

ALESSANDRA VIGANO¹

VANIA GIACOMET¹, LAURA MARTELLI¹, CLAIRE THORNE²

¹ DEPARTMENT OF PEDIATRICS, H. SACCO, MILANO, ITALY

² INSTITUTE OF CHILD HEALTH, UNIVERSITY COLLEGE LONDON, UK

e-mail: alessandra.vigano@unimi.it

phone: +39 02 39042265

fax: +39 02 39042254

Background

- We have only a limited understanding of lipodystrophy in HIV-infected children, particularly regarding epidemiology, prognosis and clinical management
- Assessment of fat redistribution in HIV-infected children is complicated by the normal, dynamic alterations in body composition that take place in childhood and puberty
- Pubertal changes in particular may complicate clinical diagnosis of lipodystrophy, as well as being a potential risk factor for the condition
- Diagnosis of lipodystrophy in children is complicated by a lack of a paediatric case definition

- Cross-sectional studies have estimated prevalence of 2-33% in HIV-infected children in Europe
- Identified risk factors for fat redistribution in HIV-infected treated children include severe HIV disease, female gender, use of protease inhibitors and use of stavudine
- There is a need for prospective studies to provide longitudinal data on lipodystrophy in HIV-infected children and adolescents

In particular, more information is needed on how lipodystrophy develops / progresses in childhood and on the clinical significance of the different types of fat redistribution and lipid/glucose abnormalities

Methods

- 55 HIV-infected children and adolescents (32 female and 23 male) identified with lipodystrophy syndrome from 12 paediatric HIV centres in Italy in a cross-sectional study in November 1999 Š November 2000 were followed up in June-November 2004
- Follow-up data were collected using standardised questionnaires; data entry and analysis were carried out in MS Access and SAS statistical software

Data collected included HIV status, current ART use, laboratory assessments of metabolic function, anthropometry and management of lipodystrophy symptoms

Definitions

Cases of fat redistribution were identified in the cross-sectional study if they had ³1 of the following signs: Peripheral lipoatrophy: Face (sunken cheeks; sunken eyes; prominent zygomatic arch), Arms or Legs (skinny; prominent veins, muscularity and bones), Buttocks (loose skin folds; prominent muscles; hollowing); Central lipohypertrophy: Trunk (increased abdominal girth), Dorso-cervix (fat accumulation, Buffalo hump); Breast (enlargement).

Combined sub-type of fat redistribution: ³ 1 sign of peripheral lipoatrophy and ³ 1 of central lipohypertrophy

Clinical assessment of body fat redistribution: Mild – only noticeable when specifically inspected; Moderate – readily obvious to the child / carer; Severe – obvious to the casual observer

Hypercholesterolemia: ³ 200 mg/dl; **Hypertriglyceridemia:** ³ 150 mg/dl

Characteristics at follow-up

Age median [range] (years)	14.1 [8.2-22.0]
Current HIV disease status (n=55)	
No / mild symptoms	15 (27)
Moderate symptoms	22 (40)
Severe symptoms	18 (33)
CD4 % (n=55)	
³ 15%	53 (96)
HIV RNA levels (n=32)	
Undetectable	18 (56)
Detectable	14 (44)
Median (copies/ml)	5,865
Current ART	
HAART	54 (98)
No treatment (discontinued)	1 (2)

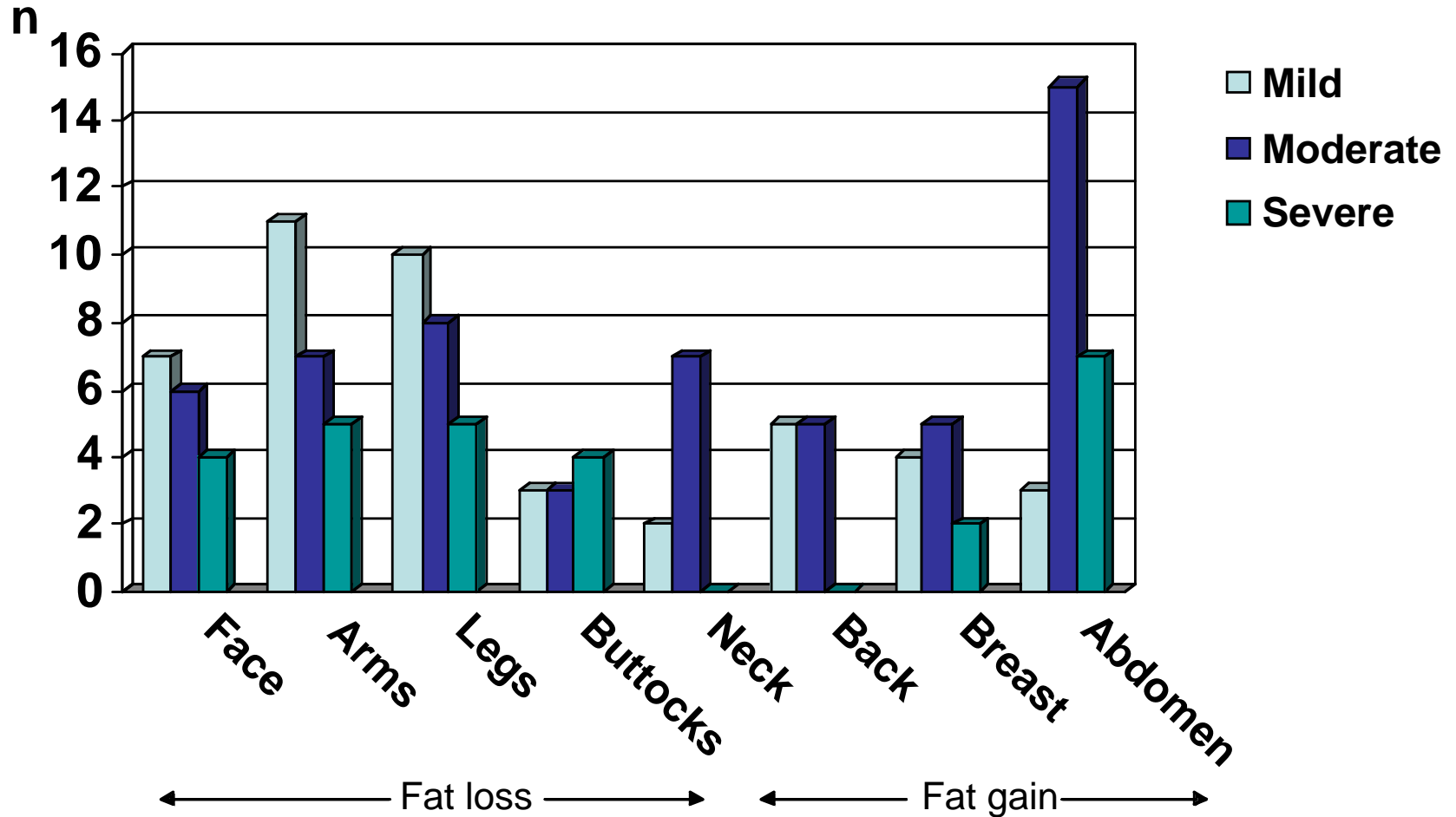
Body fat redistribution

	Combined	PLA	CLH	None
No. at follow-up (% of total cohort)	28 (51)	12 (22)	8 (15)	7 (13)
Of these group s:				
N: no change since enrollment	15 (54)	11 (92)	8 (100)	0
N: N _{progression} since enrollment	13 (46)	0	0	0
N: N _{regression} since enrollment	0	0*	0	7 (100)

Key: PLA: peripheral lipoatrophy, CLH: central lipohypertrophy

* 1 child had CLH at enrollment which regressed, but then developed PLA

Sites of body fat redistribution: Combined sub -type (n=28)



Children with regression of body fat redistribution

- 3 females and 4 males
- median age: 15.4 years (range, 12.8-21.3)
- 2 had the combined sub-type, 4 peripheral lipoatrophy and 1 central lipohypertrophy at enrollment
- one child had received recombinant human growth hormone therapy for her combined sub-type lipodystrophy since enrolment
- 1 child with prior combined sub-type had metabolic abnormalities (hypertriglyceridemia (value, 183 mg/dl))

Children with progression of body fat redistribution

- 10 females and 3 males
- median age: 15.5 years (range, 9.5 – 20.6)
- all had developed the combined sub-type at follow-up
- of the 9 with only central lipohypertrophy at enrolment:
 - 3 had severe fat gain (all in abdomen) combined with moderate fat loss (mostly in face & limbs) at follow-up
 - 1 had moderate fat gain combined with severe fat loss (in legs and arms) at follow-up
- of the 4 with only peripheral lipoatrophy at enrolment:
 - 2 had severe fat loss (limbs and buttocks) combined with severe fat gain (abdomen and breasts) at follow-up

Management of lipodystrophy symptoms

- Ten (18%) children had received drug treatment for lipodystrophy
 - 9 with recombinant human growth hormone
 - 1 with phenofibrate
- Eight had also received other interventions (3 dietary, 5 physical activity)
- One child had undergone a surgical intervention (liposuction of a Buffalo hump) during the follow-up period

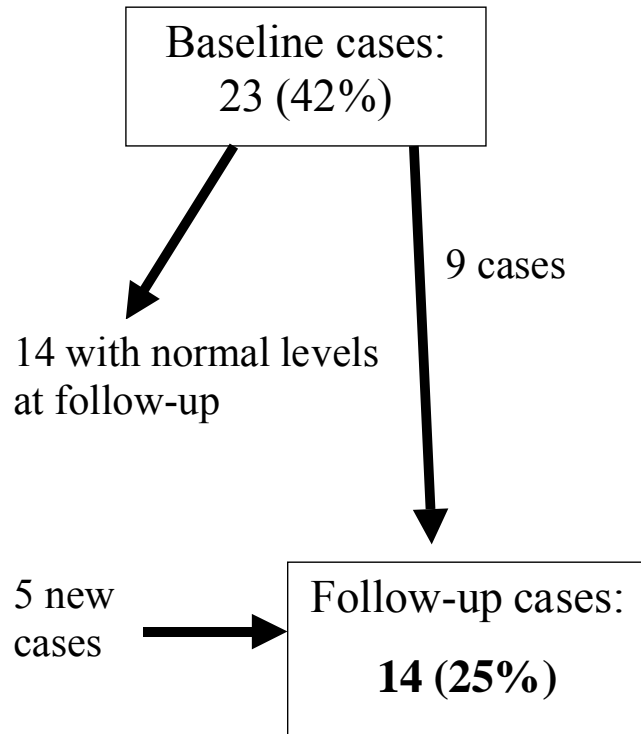
Plasma cholesterol and triglyceride levels by fat redistribution group

	Cholesterol	Triglyceride
Combined sub-type (n=28)		
Median	165 mg/dl	138 mg/dl
N (%) abnormally elevated*	7 (25)	13 (46)
Peripheral lipotrophy (n=12)		
Median	184 mg/dl	89 mg/dl
N (%) abnormally elevated	3 (25)	3 (25)
Central hyperlipotrophy (n=8)		
Median	201 mg/dl	118 mg/dl
N (%) abnormally elevated	4 (50)	2 (25)
No body fat redistribution (n=7)		
Median	143 mg/dl	72 mg/dl
N (%) abnormally elevated	0 (0)	1 (14)

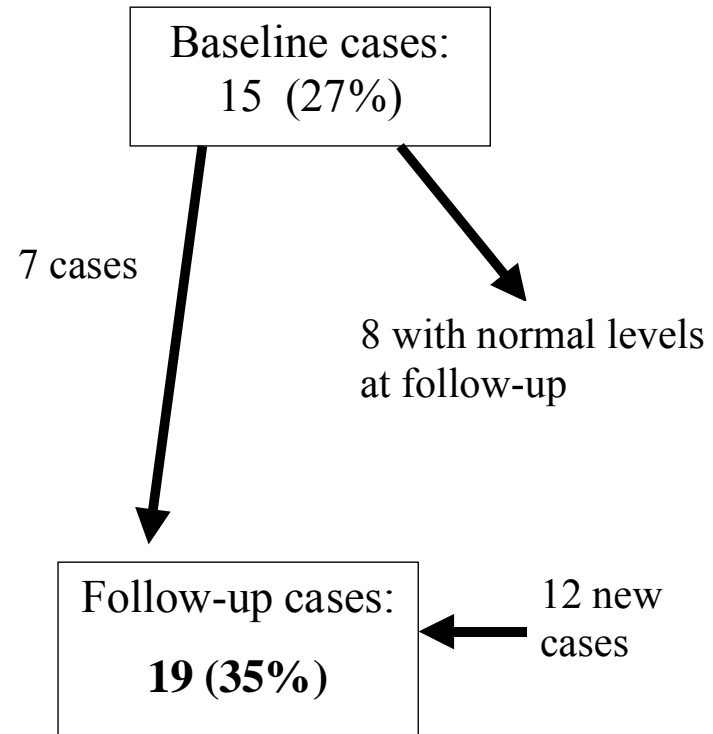
* i.e. hypercholesterolemia or hypertriglyceridemia

Metabolic abnormalities

Hypercholesterolemia



Hypertriglyceridemia



Conclusions

- Body fat redistribution arising in childhood in HIV-infected children receiving ARVs does not appear to resolve in the majority of cases
- 13% of children with body fat redistribution had no clinical signs of this by their follow-up visit (median 4 years later)
- Nearly a quarter of children showed some sign of progression with regard to fat redistribution; however this was mainly due to ~~no~~ progression to the combined sub-type rather than due to increasing severity of fat loss or fat gain

Acknowledgements

Dr Sticca (Ospedale Sant'Anna,
Como)

Prof. D. Basetti, Dr R. Rosso
(Clinica di Malattie Infettive,
Università di Genova)

Dr Lipreri, (Ospedale Cologrande,
Milano)

Dr Figini, Dr Erba, Dr Borgonovo,
Dr Brambilla, (Ospedale L. Sacco
Università di Milano)

Prof Guarino, Dr G. De Marco,
(Policlinico Federico II, Napoli)

Dr Giaquinto, Dr Ebo,
(Dipartimento di Pediatria,
Università di Padova)

Prof.ssa A.M. Maccabruni,
(Ospedale S. Matteo, Pavia)

Dr Consolini, (Clinica Pediatrica
Università di Pisa)

Dr Castelli-Gattinara, Dr Corsi, Dr
Palma, (Ospedale Bambin Gesù,
Roma)

Dr Gabiano, Dr Garetto, Dr Riva,
(Ospedale Regina Margherita,
Torino)

Dr Mazza, (Ospedale Santa Chiara,
Trento)