The challenges faced in the management of Congenital Generalized Lipodystrophy

Yasmine Abdelmeguid[1], Reham Elashry[1], Shaymaa Elsayed[1], Shaymaa Raafat[1]
[1]Pediatric Endocrinology & Diabetology Unit, Department of Pediatrics, Alexandria Faculty of Medicine, Alexandria, Egypt.

Background

- **Congenital Generalized Lipodystrophy (CGL)** is a rare autosomal recessive disease with around 500 cases worldwide.(1)
- Absence of functional adipocytes results in storage of lipids in other tissues, e.g: muscle & liver.(2)
- **Metreleptin injections** are beneficial in lowering triglycerides (TG), liver enzymes, and better glycemic control.(3) Unfortunately, it is not available in Egypt.
- We hereby report 2 cases diagnosed with CGL, and the challenges faced in their management in the absence of metreleptin.

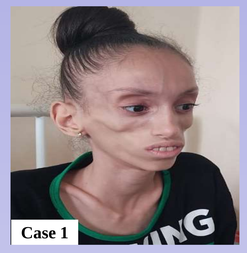
Case summary

Case 1

- A 2-year-old girl born to non-consanguineous parents presented with facial dysmorphism and loss of subcutaneous (SC) fat.
- At the age of 8 years, she had recurrent attacks of abdominal pain. Ultrasonography showed **bilateral ovarian cyst torsion**, and she had oophorectomy, and appendectomy.
- She was diagnosed clinically in our hospital with CGL at the age of **9 years**. Her TG, fasting blood glucose (FBG), HOMA-IR and liver functions were normal.
- After skipping follow up for 2 years, **xanthomas** were observed on the limbs with **severe hyperTG** (13.000 mg/dl). She was also diagnosed with **DM** (HbA1c 13%) and discharged on dietary advice, insulin, metformin, omega-3, fenofibrates & statins.
- At the age of 12 years, she complained of severe abdominal pain with shooting serum lipase, and admitted with **acute pancreatitis** due to hyperTG. CT abdomen with contrast showed pseudopancreatic cyst; which was operated.
- She continued to have recurrent attacks of pancreatitis, despite that antilipidemic treatment was maximized. Metformin had to be stopped as it was suspected to be a risk factor for pancreatitis. Her last HbA1c is 9.6% on insulin requirement 5 U/Kg/day.

Case 2

- A 12-year-old girl born to consanguineous parents was diagnosed with CGL at the age of **4 months** with typical facial features, hepatomegaly, hypertrichosis, hyperTG, and elevated liver enzymes, with normal OGTT. Her liver biopsy showed moderate macrovesicular **steatosis** and **cirrhosis**. She was given fenofibrates and statins.
- At the age of 4.5 years, she presented with precocious puberty [pubic hair (Tanner 2), breast (Tanner 1)]. Her height was 119 cm (+2.6SD), growth velocity +5SD, with advanced bone age. Her labs showed *mildly elevated DHEA-S*, normal testosterone, and 17-OH progesterone levels and was diagnosed with **premature adrenarche**.
- She was diagnosed with **DM** at age 7 years (HOMA-IR 8.1%, HbA1c 8.4%). She has good glycemic control on dietary modification, & metformin.
- Her **echocardiography** showed dilated left ventricle, depressed systolic function.

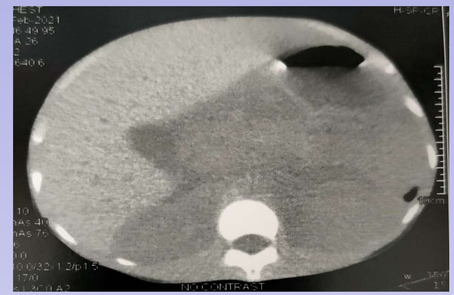

Case 1


Case 2

Photos of Case 1, and 2 showing typical facial features, loss of SC fat, triangular face, and large ears.

Clinical & Laboratory findings	Case 1	Case 2
Birth weight	2.600 Kg	**1.750 Kg**
Consanguinity	No	**Yes**
Hepatomegaly	**Yes**	**Yes**
Liver cirrhosis	No	**Yes**
Acromegaloid features	**Yes**	**Yes**
Loss of SC fat	**Yes**	**Yes**
Hypertrichosis	No	**Yes**
Acanthosis nigricans	**Yes**	**Yes**
DM	**Yes (11 years)**	**Yes (7 years)**
Last HbA1c	**9.6%**	6.9%
Treatment of DM	Insulin 5 U/Kg/day	Metformin 2000 mg/day
Occurrence of DKA	Never	Never
Hypertriglyceridemia	**Yes (SEVERE)**	**Yes (mild-moderate)**
Pancreatitis	**Yes**	No
Ovarian cyst torsion	**Yes**	No
Premature adrenarche	No	**Yes**
Cardiomyopathy	No	**Yes**

Lipid profile	Case 1	Case 2
Total cholesterol (N. < 200 mg/dl)	172	56
Triglyceride (N. < 150 mg/dl)	**1552**	**483**
HDL-cholesterol (N. > 35 mg/dl)	**12**	**5**
LDL-cholesterol (N. < 140 mg/dl)	21	6



Last CT abdomen of Case 1 showing average size of the pancreas, peripancreatic walled-off necrotic collection in superolateral aspect of the lesser sac. Liver enlarged with increased echogenicity, periportal and pericholecystic edema.

Conclusion

- Patients with CGL can be **diagnosed clinically** as their phenotypic characteristics are unique; however, different presentations and severity exist.
- Without metreleptin, **challenges are faced** affecting the quality of life and treatment should be individualized.

References

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Contact information

y_abdelmeguid17@alexmed.edu.eg