

Congenital Lipodystrophy: A Case Series Report from Cameroon

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Abstract

Congenital lipodystrophy is a group of rare syndrome characterized by the absence of subcutaneous tissue. Affecting less per million live birth, this condition associate metabolic disturbance including severe insulin resistance and progeroid appearance. Diagnosis may be fortuitous or related to complications as presented in the present case series. Lipodystrophy can be generalized or localized. Acquired lipodystrophy is associated with some drugs like antiretroviral. Thus, the condition is well described in African HIV patients but data on congenital forms from Sub Saharan Africa are sparse, justifying the present report. We present four cases, with peculiar appearance associated with increased blood triglycerides. Two on four of the patients presented diabetes mellitus. Genetic testing was not available, questioning the actual guidelines of diagnosis for our context.

Keywords

Lipodystrophy, Diabetes, Children

1. Introduction

Lipodystrophy is a group of rare congenital or acquired syndromes, characterized by generalized or partial absence of subcutaneous adipose tissue [1] [2]. This condition affects < 1 per million live births [2]. It associates various lesions including severe insulin resistance, peculiar appearance (muscular), hepatic, cardiac involvement, pancreatitis, kidney lesion [1] [2] [3] [4]. To date, more than 11 mutations in many genes are described in this condition [3]. Data on

patients from Sub Saharan Africa are sparse. This may be due to diagnosis and management difficulties despite the recent multi-society practice guideline published [2]. Acquired lipodystrophy related to antiretroviral treatment for HIV is the most frequent and thus more described in our setting [5]. The present case series describes non-HIV related lipodystrophy with the aim to show some of diagnosis difficulties in low-income countries.

2. Case Report

Two unrelated adolescents, aged 15 and 16 years old respectively, were referred from two peripheral diabetes clinics for the management of diabetes. They presented polyuria, excessive thirst, associated with uncontrolled high blood sugar (17.6 mmol for the first and 16 mmol/l for the second) despite insulin therapy. Born at term, from non-consanguineous parents, they had good adaptation to extra uterine life. Lipodystrophy was described in a cousin of one of the patient. They had normal birth weight but a peculiar appearance of generalized lipodystrophy. On physical exam, they had a generalized thin skin, acanthosis nigricans, hepatomegaly. The first case had a Tanner stage of B1P1 and the second B3P3 without menses (at 16 years). Although high insulin doses (3.8 and 3.5 UI/Kg/day), they presented persistent hyperglycemia, with increased HbA1C (14%). They both had elevated triglycerides at 240 and 230 mg/l respectively. Suggestive past history, diabetes and insulin resistance, thin skin, delay puberty and disturbance of lipid profile prompted the diagnosis of congenital lipodystrophy. The management consisted of a diet including medium chain of fatty acid, insulin therapy and metformin, in the absence of leptin.

The third case is a 5 months old infant, brought for peculiar appearance. Born at term, from non-consanguineous parents, she had a voracious appetite contrasting with stunting. On physical exam, she had a very thin skin and hepatomegaly and generalized thin skin. She had 535 mg/L of triglycerides. The fourth case is a male infant, addressed at 4 months old for further management of elevated blood triglycerides. This was a fortuitous discovery during a routine blood analysis for malaria and otitis media. The milky aspect of blood prompted the realization of lipid profile. The child is the third, born at term from non-consanguineous parents. The infant presented a psychomotor delay (Denver score 2 months), stunting despite a conserved appetite, umbilical hernia and discrete lipodystrophy (head and neck). The lipid profile revealed total blood cholesterol five times normal (146.8), elevated blood triglycerides at 200 g/l. Elevated lipasemia (1056UI/L) was suggestive of pancreatitis. Management of these infants includes exclusive breast milk up to 6 months, followed by the introduction of medium chain polyunsaturated fatty acid in feeding during diversification. A control of a number of feeding was also an important part of her nutritional management.

A careful follow up of these patients was initiated to early identify complications. Genetics testing was not available. **Table 1** summarizes clinical features of the patients.

Table 1. Clinical findings of the four cases.

Patient Number	Age at diagnosis (year)	Birth weight (g)	Circumstance of diagnosis	Weight(SDS)	Height(SDS)	Site	Triglyceride level (mg/l)	Other findings
1	15	3350	Diabetes	-1	+1	Generalized	240	Pubertal delay, liver enlargement
2	16.4	3400	Diabetes	-1	+2	Generalized	230	Pubertal delay, liver enlargement
3	0.41	3550	Progeroid appearance	-2	-1.8	Generalized	535	Liver enlargement
4	0.4	3100	Fortuitous	-2.3	-2	Localized	200	Psychomotor delay, hypotonia

3. Discussion

Lipodystrophy or lipoatrophy are heterogeneous rare conditions characterized by fat loss [1]. This report is the first describing patients in a pediatric population from Cameroon. In our case series, we had three girls and a boy. This is consistent with literature where the sex ratio is in favor of females. A family history was found in a patient, from non-consanguineous family. Even though these are recessive disorders, consanguinity is not found in more than 40% of cases [1].

Age at diagnosis is variable in literature. It is earlier in patients with congenital generalized lipodystrophy than in other forms of lipodystrophy. Our patients presented early-generalized muscular appearance but diagnosis was made at 15 and 16 years through diabetes in two of them. On contrary, the two others were diagnosed at 4 and 5 months respectively. Thus, misdiagnosis may be common in our setting especially for partial forms of lipodystrophy [1] [2].

Infectious illness preceding diagnosis was found in a patient. This is described in 25% to 85% of patients in literature. The most frequent organ involved during illness is liver [1]. Hepatomegaly is found in up to 80% of patients, due either to fatty liver or autoimmune hepatitis [1] [6]. In our series, three patients on four presented with liver enlargement at diagnosis. Neurological disorders are less common, but some teams described epilepsy, intellectual disability [3] [7]. One of our patient present with a psychomotor delay despite a good adaptation to extrauterine life excluding anoxic encephalopathy. This feature is rare in literature. On the contrary, increased appetite, reported in three of our patients, affects half of patients with CGL, contrasting with growth retardation especially in infants. [1] [8]. Endocrine disorders can be part of the disease, especially in adolescent and adults. This is the case in our oldest patients. They had diabetes with severe insulin resistance, pubertal delay, and growth retardation. It is possible to find also polycystic ovaries in adolescent girls [1] [2]. Heart and kidney lesions are also fearsome complications of the disease.

High blood triglyceride level was unsurprisingly a common feature in the four cases. Diagnosis of lipodystrophy should be confirmed by molecular analysis. The latter is not available in low-income countries. Therefore, presumptive di-

agnosis needs a clinical and biochemical algorithm to helps physician in low-income countries, to evokeproperly diagnosis. Evidence of association of thin skin testifying fat loss, resulting in a muscular appearance (generalized or partial, prominent veins), insulin resistance (hypertriglyceridemia, acanthosis nigricans, diabetes mellitus in a child is concordant with diagnosis [1] [2]. A careful past history enquiry may help to exclude acquired lipodystrophy [2].

Diet with medium chain fatty acid and omega 3 plays a key role in the management of affected patients, with good metabolic results in some teams [9]. Metformin is useful to reduce insulin resistance [10]. Leptin is not routinely available in low-income countries.

Multiple organ involvement gives the disease a multi-systemic character, which are severity criteria during follow-up. However, molecular analysis is necessary to identify the type of gene lesion present in our context.

4. Conclusion

We presented four cases of non-HIV related lipodystrophy from Cameroon. Clinical features and lipid profile oriented the diagnosis. The entry for diagnosis may vary from fortuitous in an infant with a febrile illness to diabetes. However, molecular analysis was not done and the question of the type of gene mutation involved in our population is unanswered. Thus, international collaborative studies to improve understanding, management of affected patients are required.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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