Case Report

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A Patient with Congenital Generalized Lipodystrophy

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Received: 28 October 2021 **Revised:** 23 November 2021 **Accepted:** 29 December 2021

ARTICLE INFO

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Keywords:
Autosomal recessive,
Hepatomegaly,
Lipodystrophy,
Lymphadenopathy

ABSTRACT

Background: Congenital generalized lipodystrophy (CGL) presents during the first two years of life. It is a rare autosomal recessive inherited disease with loss of cutaneous fat and various complaints and complications such as diabetes mellitus, hypertriglyceridaemia and hepatic steatosis.

Case Report: A patient was hospitalized with abdominal distention, weight loss, irritability, and pruritus. Massive hepatomegaly, huge splenomegaly, multiple significant lymphadenopathies, hypertrichosis, generalized subcutaneous fat loss with bird-faced, increased musculature, and prominent superficial veins were detected on examination. In paraclinical evaluation, hyperlipidemia and severe liver fibrosis (grade 5) were diagnosed, and she was discharged as a case of congenital generalized lipodystrophy.

Conclusion: In an approach to a child with hepatosplenomegaly, lipodystrophy should be in mind.

Introduction

Lipodystrophy is a rare group of heterogeneous lipid and carbohydrate metabolism disorders characterized by variable loss of adipose tissue.[1] Loss of body fat may affect the whole body (generalized), specific areas of the body (partial), or small areas of subcutaneous fat (localized).[2] This disorder can be caused by underlying genetic defects (genetic lipodystrophy) or autoimmune mechanisms (acquired lipodystrophy) or medications such as antiretroviral drugs or human immunodeficiency virus [HIV].[3,4]

One of the main types of genetic lipodystrophy is congenital generalized lipodystrophy (CGL), or Berardinelli-Seip syndrome that is an autosomal recessive disorder.[2] The prevalence of CGL is one in 10 million people.[5] This disorder is characterized by losing entire body fat tissue at birth or in the first year of life. Most

patients are diagnosed with significant loss of fat and subsequent muscles and subcutaneous vein prominence in the first year of life or early childhood. However, some patients without access to regular medical care may be diagnosed later in life and may rarely be identified with acromegaly symptoms such as enlarged hands, feet, and jaws in adulthood.[5-7]

Patients with CGL characterized by hepatomegaly, splenomegaly, hypertrophic cardiomyopathy, dyslipidemia (increase in triglycerides, decrease in HDL), Hyperinsulinemia, and insulin resistance cause the development of acanthosis nigricans. Hepatic steatosis is common in these patients and can lead to steatohepatitis, cirrhosis, and liver failure.[2,8] Female patients with CGL may experience symptoms such as clitoromegaly, hirsutism, irregular menstrual cycles, polycystic ovaries, and/or infertility.[2,9]

Case Report

A four-year-old Iranian girl was admitted with abdominal distention, weight loss despite increased appetite, irritability, and fever. She was the second child of consanguineous parents. On examination, weight was 13.5 Kilograms, and height was 100 Centimeter. Blood pressure, pulse rate, respiratory rate, and temperature were in the normal range. No fever was detected during hospitalization. Massive hepatomegaly, huge splenomegaly, significant neck lymphadenopathies, hypertrichosis, prominent superficial veins, subcutaneous fat loss with bird-faced, and increased body musculature were abnormal findings in physical examination (Figure 1). The patient's laboratory findings are in Table 1.

Trans-abdominal ultrasonography showed hepatosplenomegaly and a moderately increased echo of both kidneys' parenchyma. Evidence of malignancy wasn't seen in bone marrow aspiration, but dyserythropoietic's change was confirmed. Her bone age was two years old, according to the wrist X-ray.

Figure 1. Hepatosplenomegaly, neck lymphadenopathies, hypertrichosis, prominent superficial veins, subcutaneous fat loss with bird-faced, and increased body musculature are positive findings of the presented patient

Liver biopsy showed mononuclear infiltration in portal tracts, piecemeal necrosis, feathery degeneration, and fibrosis stage 5 (Figure 2). Cervical Lymph node excisional biopsy revealed follicular hyperplasia.

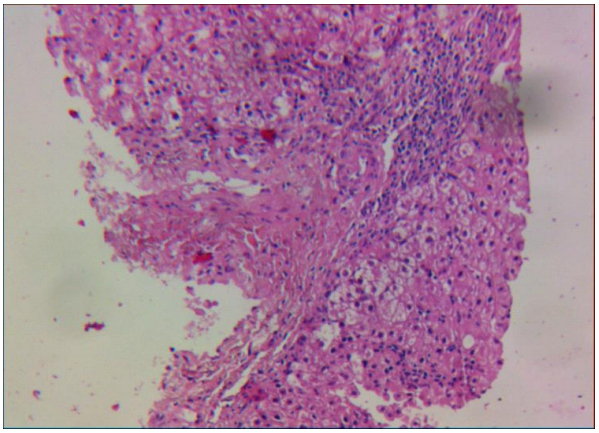

Figure2. Liver biopsy shows mononuclear infiltration in portal tracts, piecemeal necrosis, feathery degeneration, and fibrosis stage 5

The final diagnosis was congenital generalized lipodystrophy, and the patient was discharged with a recommendation on low carbohydrate, low-fat diet, and periodic follow up for diabetes, hyperlipidemia, and complications of chronic liver disease.

Table 1. Laboratory Findings

Parameter	Patient	Normal value
White Blood Cell (/millimeter^3)	6.5 x 10^3	3.54-9.06 x 10^3
Hemoglobin (Gram/deciliter)	10.5	13.3-16.2
Platelet (/millimeter^3)	234	165-415 x 10^3
Protrombine Time (second)	12	12.7-15.4
Erythrocyte Sedimentation Rate (millimeter/hour)	5	0-20
AspartateTransaminase (unit/Liter)	97	7-41
Alanine Transaminase (unit/Liter)	194	7-41
Alkaline Phosphatase(unit/Liter)	844	33-96
Total Bilirubin (milligram/deciliter)		0.3-1.3
Direct Bilirubin (milligram/deciliter)		< 0.3
Albumin (gram/deciliter)	5.1	4.1-5.3
Human Immunodeficiency Virus Antibody	Negative	Negative
Fibrinogen (milligram/deciliter)	180	233-496
Blood Culture	Negative	Negative
Thyroid Stimulating Hormone (IU/mL)	3.1	0.34-4.25
Blood Urea Nitrogen (milligram/deciliter)	14	7-20
Fasting Blood Sugar (milligram/deciliter)	110	75-100
Triglyceride (milligram/deciliter)	705	30-200
Cholesterol (milligram/deciliter)	181	< 240
Antinuclear antibody	Negative	Negative
Anti-liver kidney microsome antibody	Negative	Negative
Anti-smooth-muscle antibody	Negative	Negative
Vitamin D total (ng/ml)	13/5	4.8-52.8
Calcium (Ca)(mg/dl)	10.3	8.6-10.3
Complement 3 (milligram/deciliter)	89	83-177
Complement 4 (milligram/deciliter)	28	16-47
Immunoglobulin A (milligram/deciliter)	41	70-350
Immunoglobulin E (milligram/deciliter)	16	10-179
Immunoglobulin G(milligram/deciliter)	1124	700-1700
Immunoglobulin M (milligram/deciliter)	111	50-300
Urine analysis	Normal	Normal

Discussion

Lipodystrophies are a group of congenital disorders characterized by abnormal fat tissue deposition and are often associated with metabolic complications such as insulin resistance, dyslipidemia, fatty liver with hepatic dysfunction, hypertrophic cardiomyopathy, muscular hypertrophy, and various endocrine disturbances. The congenital generalized lipodystrophy diagnosis is based on clinical findings: reduction of total adipose tissue, muscular hypertrophy, and prominent superficial veins. Also, laboratory findings can show hypertriglyceridemia and diabetes with severe insulin resistance.

Our patient was also presented with general lipodystrophic features such as subcutaneous fat loss, muscle gain, hypertrichosis, prominent superficial veins, increased appetite and hepatosplenomegaly.

Our patient had normal intelligence. Although a few cases with cerebellar degeneration and neurodegenerative disease have been reported[10], and some patients have mental retardation[11], most patients have normal intelligence.

Liver disorders in lipodystrophy range from abnormal LFT to adipose tissue infiltration, hepatomegaly, hepatic steatosis, and cirrhosis. Results of our patient's liver biopsy showed mononuclear infiltration in the portal tract, piecemeal necrosis, and severe fibrosis (stage 5).

Congenital generalized lipodystrophy might be associated with several skin disorders such as severe acanthosis nigricans, generalized hyperpigmentation, curly scalp hair[12], dermatomyositis[13], and scleroderma. Our

patient had pruritis and skin bulla formation.

In laboratory findings, our patient had hyperlipidemia; her serum Triglyceride level was 705 milligram/deciliter. Some patients with lipodystrophy, especially after the onset of insulin-resistant diabetes, develop severe hypertriglyceridemia following a recurrence of acute pancreatitis attacks.[14,15]

Although there is no definitive treatment for lipodystrophy, complications, and mortality improve with early intervention.[2] The basis of lipodystrophy treatment is the management of metabolic abnormalities to prevent complications. In order to prevent the acceleration of hepatic steatosis and worsening diabetes and hyperlipidemia, overfeeding should be avoided, especially in infants and children. Physical activity should also be increased to improve comorbidities, except in those patients with contraindications such as severe cardiomyopathy.[16]

Treatment strategies for hypertriglyceridemia include medium-chain triglyceride-based formulas in infants and low-fat diets in older patients.[17] Treatment of patients with insulin resistance and diabetes uses oral drugs and insulin.[2]

Conclusion

Lipodystrophy should be considered when approaching a child with hepatosplenomegaly and a wide range of clinical presentations.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

The authors would like to thank the patient's family for their cooperation in this study.

The present study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.MEDICINE.REC.1400.336).

How to Cite: Edalatkhah R, Baghbanian M. A Patient with Congenital Generalized Lipodystrophy. World J Peri & Neonatol 2022; 5(1): 40-4.
DOI: 10.18502/wjpn.v5i1.10127

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