A Case with Lipoid Proteinosis Intersected with Diabetes Mellitus

Lipoid Proteinosis ve Diabetes Mellitusun Kesiştiği Bir Olgu

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Abstract
Lipoid proteinosis (LP) is a rare disorder inherited as an autosomal recessive trait. LP is characterized by deposition of hyaline-like material in the skin, mucous membranes, and other tissues. LP has been mapped to chromosome 1q21, the locus for the extracellular matrix protein 1 (ECM1) gene. In this case report, we aimed to present a case with LP accompanied by diabetes mellitus, and to discuss the possible mechanisms of diabetes in LP. A 16-year-old girl presented to the endocrinology department with hyperglycemia. She reported a history of progressive hoarseness of her voice since she was two years old. Our patient meets the clinical and histopathological criteria for the diagnosis of LP. Her fasting glucose was 310 mg/dl. Plasma insulin and C-peptide levels were 5.1 uU/ml and 1.57 ng/ml, respectively. Hemoglobin A1c was 12.3%. HOMA-IR (Homeostasis Model Assessment-Insulin Resistance) ratio was 3.1 (normal range <3.7). Serum islet cell antibodies, anti-GAD antibodies and anti-insulin antibodies were negative. Diabetes mellitus was diagnosed and insulin treatment was initiated. In conclusion, possible mechanism of diabetes mellitus may be result of the diffuse deposition of amorphous material into the capillary vessels or in pancreas. The other possible mechanism responsible for the association of diabetes mellitus and insulin resistance in LP patients may be sharing a mutation at 1q21 locus. Future studies which aimed screening of insulin resistance and diabetes mellitus in LP patients may be helpful to explain this association. Turk Jem 2009; 13: 60-2

Key words: Lipoid proteinosis, diabetes mellitus

Özet

Anahtar kelimeler: Lipoid proteinosis, diabetes mellitus

Introduction
Lipoid proteinosis (LP), also known as hyalinosis cutis et mucosae, was first described by a Viennese dermatologist and otorhinolaryngologist, Urbach and Wiethe, in 1929 (1). Indeed, the condition is also sometimes referred to as Urbach-Wiethe disease. Since their report, over 300 cases of this disorder have been described. Lipoid proteinosis is a rare disorder inherited as an autosomal recessive trait. Recently, lipoid proteinosis has been mapped to chromosome 1q21, and the locus for the extracellular matrix protein 1 (ECM1) gene and six different mutations in the ECM1 gene have been identified in patients affected by LP (2). LP is characterized by deposition of hyaline-like material in the skin, mucous membranes, and other tissues (3,4). Clinical manifestations may occur as early as in the first 2 years of life, and are the result of skin and mucous membrane changes (5). Histologically, LP

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is characterized by periodic acid-Schiff (PAS)-positive, but diastase-resistant, basement membrane thickening at the dermal-epidermal junction, surrounding blood vessels and adnexal epithelia, as well as deposition or accumulation of hyaline material in the dermis [6]. Immunofluorescence labelling with anti-type IV collagen antibody shows bright, thick bands of staining at the dermal-epidermal junction and around blood vessels consistent with basement membrane thickening. In addition, dermal fibroblasts demonstrate characteristic cytoplasmic vacuole formation [7]. Autopsy studies have shown LP to be a generalized disorder with microscopic deposits of hyaline material in practically every organ. However, clinical manifestations of endocrine disorders have been described only in two LP patients who had insulin resistance [8]. In this case report, we aimed to present a case with LP accompanied by diabetes mellitus, and to discuss the possible mechanisms of diabetes in LP.

Case Report

A 16-year-old girl presented to the endocrinology department with hyperglycemia. Body weight and height of the patient were 37.1 kg and 149 cm, respectively. Body mass index was 16.7 kg/m². Waist circumference was 65 cm and blood pressure was 110/80 mmHg. Her fasting glucose was 310 mg/dl. Plasma insulin and C-peptide levels were 5.1uU/ml and 1.57 ng/ml, respectively. Hemoglobin A1c was 12.3%. HOMA-IR (Homeostasis Model Assessment-Insulin Resistance) ratio was 3.1 (normal range<2). Serum islet cell antibodies, anti-GAD antibodies and anti-insulin antibodies were negative. Diabetes mellitus was diagnosed and insulin treatment was initiated. She was born to consanguineous parents. Family history revealed a presence of 6 brothers and 3 sisters. Moreover, LP was diagnosed in one of the sisters who had similar morphological features with our patient, but she had normoglycemia. She reported a history of progressive hoarseness of her voice since she was two years old. She had suffered from progressive skin and mucous membrane changes on her face, abdomen, back, legs and eyelids since early childhood. Physical examination revealed multiple acneiform scars on her face (Figure-1), abdomen, back, legs, and multiple beaded papules on the eyelids, hyperkeratosis of the hands. Yellow-white infiltrations were observed on oral mucosa and tongue. The oral mucosa was nodular and thickened, with primary involvement of the labial, buccal and palatal mucosa, posterior tongue, the palate and the back wall of the pharynx. Oral and laryngeal mucosae were fibrotic and thickened. Moreover, the infiltrates in her tongue and its frenulum were limiting lingual movements and were causing speech difficulties. Laryngoscopic examination showed hyperemic edematous vocal cords. Retinal examination was normal. Skin biopsy of the lesions was concordant with LP. Complete blood count, sedimentation rate, liver and renal functions were within the normal ranges. Her lipid profile was as follows: triglyceride 114mg/dl, total cholesterol 222 mg/dl, LDL 159 mg/dl, HDL 53 mg/dl, VLDL 18 mg/dl. Electrocardiography and Doppler echocardiography were normal. Metabolic screening, thyroid function tests, and electroencephalogram were also normal. The patient appeared mentally normal and did not show any calcifications on skull X-rays and cranial computed tomography imaging. Pancreatic magnetic resonance imaging showed no pathology.

Discussion

No laboratory finding is typical of LP except for the histopathological findings. Our patient meets the clinical and histopathological (Figure-2) criteria for the diagnosis of LP. In addition she was diagnosed as diabetes mellitus. Existence of type 2 DM in subjects with LP has not been reported previously. We encountered two sisters with insulin resistance (8) and one type 1 DM patient with LP. The authors thought that LP with type 1 DM might be coincidental [9]. LP is characterized by deposition of hyaline-like material in many tissues [3,4]. Therefore, we can speculate that DM in our patient may be secondary to the deposition of hyaline-like material in pancreas or capillary vessels. However, we could not demonstrate any radiological finding on magnetic resonance imaging of the pancreas. The deposition of hyaline-like material in capillary vessels was accused for insulin resistance in subjects with LP [8]. HOMA-IR was normal in our subject; hence, hepatic insulin resistance may not be responsible for DM in our case. Recently, LP has been mapped to chromosome 1q21, and the locus for the extracellular matrix protein 1 (ECM1) gene and six different loss-of-function mutations in the ECM1 gene have been identified in patients affected by LP [2] Notably, the ECM1 gene product is an 85-kDa glycoprotein of unknown function that is believed to affect keratinocyte differentiation, and it is possible that it has a role in cell-cell adhesion [10]. On the other hand, some studies showed that the region on chromosome 1q21-q24 was significantly linked to type 2 diabetes [11]. Although we could not perform genetic analysis, 1q21 gene locus may be related to DM and LP at the same time in our case.
Conclusions

1. Possible mechanism of diabetes mellitus may be result of the diffuse deposition of amorphous material into the capillary vessels or in pancreas.
2. The other possible mechanism responsible for the association of diabetes mellitus and insulin resistance in LP patients may be sharing a mutation at 1q21 locus.
3. Future studies which aimed screening of insulin resistance and diabetes mellitus in LP patients may be helpful to explain this association.

References