

# Type 2 diabetes mellitus: An unusual association with Down's syndrome

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Down's syndrome (DS) is known to be associated with autoimmune disease including type 1 diabetes. To the best of our knowledge, there are no reports of DS with type 2 diabetes mellitus in the literature. We hereby report two cases of DS with type 2 diabetes.

**Key words:** Down's syndrome, type 2 diabetes, autoimmune

## Introduction

Down's syndrome (DS) is one of the common chromosomal disorders and the most common cause of mental retardation. It is well-known that patients with DS have an increased prevalence of autoimmune disorders affecting both endocrine and non-endocrine organs.<sup>[1]</sup> Although cases of DS associated with diabetes mellitus (DM) have been reported in the past, invariably all cases were associated with type 1 DM.<sup>[2-4]</sup> We present two cases of type 2 DM with DS and believe that this is the first report of type DM with DS.

## Case Reports

### Case 1

A 28-year-old male patient with a body mass index (BMI)

of 25.1 kg/m<sup>2</sup> and positive family history of DM reported to the out-patient clinic of the department of Endocrinology, Medwin hospital with the clinical features of polyuria and polydipsia for last 1 year. There was no history of weight loss or any significant past medical history. Physical examination revealed typical mongolian facies and other features of DS such as short stature (145 cm), brachycephaly, short neck and pot belly, small mouth with protruding tongue, wide occipital region and characteristic small eyes of DS. Thyroid was not palpable. Laboratory data revealed diabetes with fasting plasma glucose of 256 mg/dl, postprandial plasma glucose of 375 mg/dl and glycated hemoglobin (HbA1C) level of 9.9%. Urine was negative for ketone bodies. C-peptide assay showed fairly well-preserved pancreatic  $\beta$  cell function: Fasting values of 1.3 pmol and stimulated values of 2.4 pmol/ml (normal values in non-diabetic subjects, fasting >1.5 pmol/ml and stimulated >4.0 pmol/ml). Glutamic acid decarboxylase (GAD) antibody testing (3.2 IU/ml) was negative. These values were suggestive of type 2 DM. He also had primary hypothyroidism with a thyroid stimulating hormone level of 54 mIU/l and T<sub>4</sub> value of 3.5  $\mu$ g/dl. Other investigations (hemogram, renal and liver function parameters, serum electrolytes and lipid profile) were within the normal limits. He was initiated on basal glargine insulin at a dose of 15 units subcutaneously at night along with oral hypoglycemic agent (glimepiride 2 mg/metformin 1000 mg) once daily and L-thyroxine 100  $\mu$ g daily. Later, the doses of insulin were reduced and subsequently withdrawn completely and he is maintained well on oral hypoglycemic agents alone.

### Case 2

A 26-year-old female patient with a BMI of 33.4 kg/m<sup>2</sup> with

Access this article online	
Quick Response Code:	Website: www.ijhg.com
	DOI: 10.4103/0971-6866.120818

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strong family history of DM were admitted in the in-patient Department of Endocrinology, Medwin Hospital for proper control of hyperglycemia. She gave a history of polyuria, but denied any weight loss. Physical examination revealed features of DS (short stature, obesity, brachycephaly, gynecomastia, protruding tongue, simian crease, pot belly, short neck and acanthosis nigricans, wide occipital region with characteristic small eyes). The laboratory evaluation revealed fasting and postprandial sugar levels as 175 mg/dl and 240 mg/dl, respectively HbA1c of 8.9%. Urine was negative for ketones. His fasting and stimulated C-peptide levels were 1.4 pmol/ml and 2.5 pmol/ml with negative GAD-antibody test (4.1 IU/ml). Other investigations were within normal limits. Glycemic control was achieved with gliclazide 40 mg with metformin 500 mg twice daily.

## Discussion

Previous studies had suggested that type 1 DM is more prevalent in people with DS than in the general population and vice versa.<sup>[5,6]</sup> To the best of our knowledge, this is the first report of DS associated with type 2 DM.

Impaired  $\beta$  cell function and insulin sensitivity are the main factors in the pathogenesis of type 2 DM.<sup>[7,8]</sup> B cell function was fairly preserved in these two patients (as indicated by C-peptide levels in the blood) with negative antibody testing for GAD-Ab. This indicated toward the fact that impaired insulin sensitivity might have contributed to a greater extent in the development of type 2 DM in these two patients.

A variety of genetic syndromes have been described in which DM occurs with increased frequency.<sup>[9-11]</sup> The etiology of the disturbance in glucose homeostasis in these diverse and unrelated syndromes remain undefined. Since rare forms a disease often provide insight into the possible mechanisms of the disease and since each candidate gene contributes a small amount of genetic risk to the disease, individuals with DS and type 2 DM may therefore provide the clinical insights into possible mechanisms underlying susceptibility to diabetes.

## Conclusion

Further investigations are warranted to prove whether the presence of type diabetes in patients with DS was a chance association or whether there is a genetic basis for this association. However, these two cases point to the fact that one should screen patients with DS for type 2 diabetes.

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**Cite this article as:** Kota SK, Tripathy PR, Kota SK, Jammula S. Type 2 diabetes mellitus: An unusual association with *Down's syndrome*. *Indian J Hum Genet* 2013;19:358-9.

**Source of Support:** Nil, **Conflict of Interest:** None declared.