Polyglandular Autoimmune Endocrinopathy in Type 2 Diabetes

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Abstract
Polyglandular autoimmunity (PGA) type 2 presenting in childhood is extremely rare. We report a case of type 2 PGA who had hypothyroidism, followed by diabetic ketoacidosis and was later diagnosed to have adrenal insufficiency also.

INTRODUCTION
Polyglandular autoimmunity (PGA) type 2 is a rare syndrome characterized by autoimmune thyroid disease, hypoadrenalism and type 1 diabetes. Presentation of the disease in childhood, as in this case report, is even more uncommon and for this reason it merits reporting.

CASE REPORT
A 15 year young boy presented with sudden onset of unconsciousness and was referred to Endocrine Unit of the hospital with blood glucose level of 450 mg/dl. He had history of polyuria, polydipsia and vomiting for 5 days. Four years ago, he had been diagnosed to have primary hypothyroidism, as he presented with symptoms, such as cold intolerance, weight gain, muscle cramps and goiter (TSH was 22 mIU/ml). He had been on regular thyroxin replacement (100 µg/day) since then with amelioration in the symptoms.

On physical examination, he was comatosed, pulse rate was 102/min and BP was 80/60 mm Hg. He had marked dehydration, pallor and acidotic breathing with goiter. Axillary and pubic hairs were absent and genitalia was prepubertal. His weight was 30 kg (BMI 18.3 kg/m²) and height was 129 cm (< 3rd percentile of ICMR growth chart). The height age was 11 years and bone age was 9 years. Skin pigmentation was unremarkable. Systemic examination revealed tachycardia with normal chest and cardiovascular findings.

Both pupils were normal in size and reacting to light. Plantar reflexes were bilaterally extensor with normal deep tendon reflexes and other superficial reflexes. There were no signs of meningeal irritation. Fundus examination under full mydriasis was normal.

The investigations revealed haemoglobin - 11 gm/dl, total leukocyte count 19300/mm³ (neutrophils - 72% lymphocytes - 35% and eosinophils - 3%), blood urea 105 mg/dl, serum creatinine - 1.1 mg/dl, serum Na⁺ - 145 meq/l, K⁺ 5.4 meq/l, total serum protein 6.7 g/dl, serum albumin 2.1 g/dl (due to his illness and protein energy malnutrition), 24 hr urinary protein - 135 mg/24 hr, blood sugar - 450 mg/dl. Urine was positive for ketone bodies and chest roentgenogram was normal. Serum Anti TPO antibody was positive (> 100 IU/ml by RIA).

He was managed for diabetic ketoacidosis. Presence of two endocrine organ failure preempted us to undertake the insulin-induced hypoglycemia test for assessing adrenal reserve. Serum cortisol was 5.6 µg/dl at baseline and was 6.6 µg/dl after 60 min of insulin injection (0.1 unit/kg body weight) to induce hypoglycemia (blood glucose < 40 mg/dl). This indicated diminished adrenal reserve. There days later, Synthetic ACTH (Synacthen) 250 µg was given intravenously and serum cortisol samples were collected at 0 and 60 minutes. Serum cortisol failed to rise after synacthen injection, confirming primary adrenal insufficiency. The patient was discharged on L-thyroxine 100 µg/day, insulin 40 units/day and prednisolone - 5 mg/day (in two divided doses).

DISCUSSION
Polyglandular endocrine syndrome is a rare disease in which HLA-associated genetic predisposition coupled with environmental factors trigger an autoimmune process which may result in glandular hypofunction or hyperfunction. Type 2 PGA is the commonest amongst all types of polyglandular endocrinopathy and it manifests in the middle decades of life. Adrenal insufficiency, type 1 diabetes and autoimmune thyroiditis are predominant. Adrenal insufficiency is usually the first to manifest, followed by autoimmune thyroiditis and type 1 diabetes, but the appearance of endocrinopathy can follow any order. Other associations are vitiligo, celiac disease, pernicious anemia, hypogonadism and alopecia.

Type 2 PGA presenting in childhood is rare. In world literature, the youngest case reported to occur was in a young
child of 8 years. Our patient is the second case report of type 2 PGA occurring in childhood and first of its kind in India (literature search MeSH year 1980-2003). In our patient, autoimmune thyroiditis manifesting as hypothyroidism was first to appear at the age of 11 years, followed by type 1 M (ketoacidosis) and adrenal insufficiency. His growth and sexual maturation were adversely affected due to hypothyroidism. Irregular treatment and subsequent development of adrenal insufficiency might have contributed to failure of “catch-up” growth which occurs in children with hypothyroidism on thyroxine replacement. This case presented with primary hypothyroidism and within four years of onset, he developed beta cell failure and adrenal insufficiency, which suggests a relatively faster progression of polyglandular involvement of endocrine glands. Other members of the family did not suffer from a similar illness. A point mutation occurring in gene regulating region is speculative. Monitoring of the growth velocity and biochemical improvement were important aspects for consideration in follow up of the case.

REFERENCES


Announcement

The Vth National Conference of Indian Leptospirosis Society will be organized at Govt. Medical College, Surat, Gujarat from January 20-22, 2005.

The conference includes guest lectures, free-paper and post-paper presentations on various aspects on leptospirosis, plenary sessions etc.

Interested persons may please contact: Dr. Vikas K Desai, Organizing Secretary of the Conference (Head, Department of Community Medicine, Govt. Medical College, Surat, Gujarat Phone: 0261 3244529; E-mail: cmdgmcs@hotmail.com for further information.