Autoimmune Polyendocrine Syndrome 2 in A Child – A Case Report

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Case History

- 11 years old child Dinesh kumar second child to 3rd degree consanguineous parents.
- Diagnosed with diabetes at age of 7 years
- Severe DKA at presentation.
- Followed up in diabetic clinic past 4 years.

Contd..

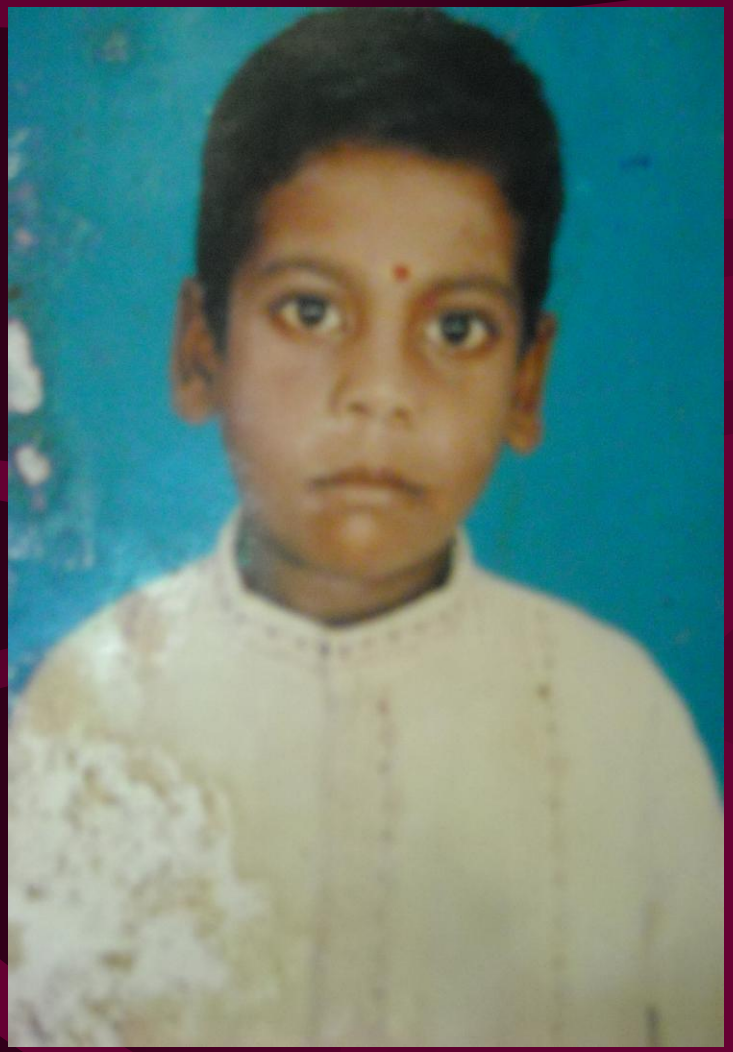
- One admission for DKA in past 4 years, otherwise uneventful.One episode of Acute viral hepatitis A one year back.
- Developed hypoglycemic episodes 4 years after being diagnosed.
- Necessitated insulin dose reduction by 25%
- Increased pigmentation of face and upper limb for two months duration.

Contd..

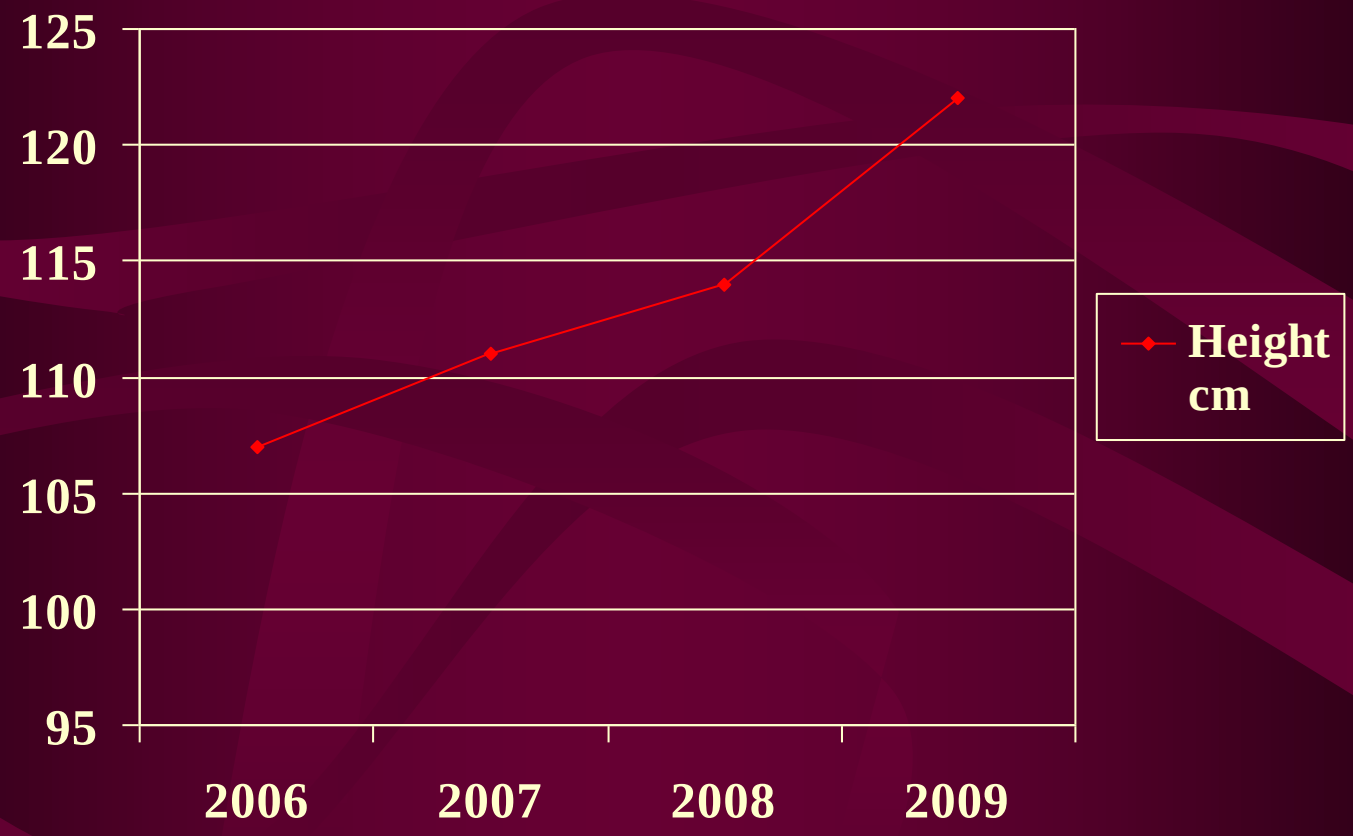
- No family history of Addison disease , Diabetes mellitus or other endocrine disorders.
- No h/o contact with T.B.

Clinical Examination

- Increased pigmentation over face, upper limbs, trunk, creases.
- Genitals normal.
- He was normotensive.
- No acanthosis, no vitiligo, no goitre,no alopecia.
- Other systems examination normal.
- No signs of Vitamin deficiencies.



Growth pattern



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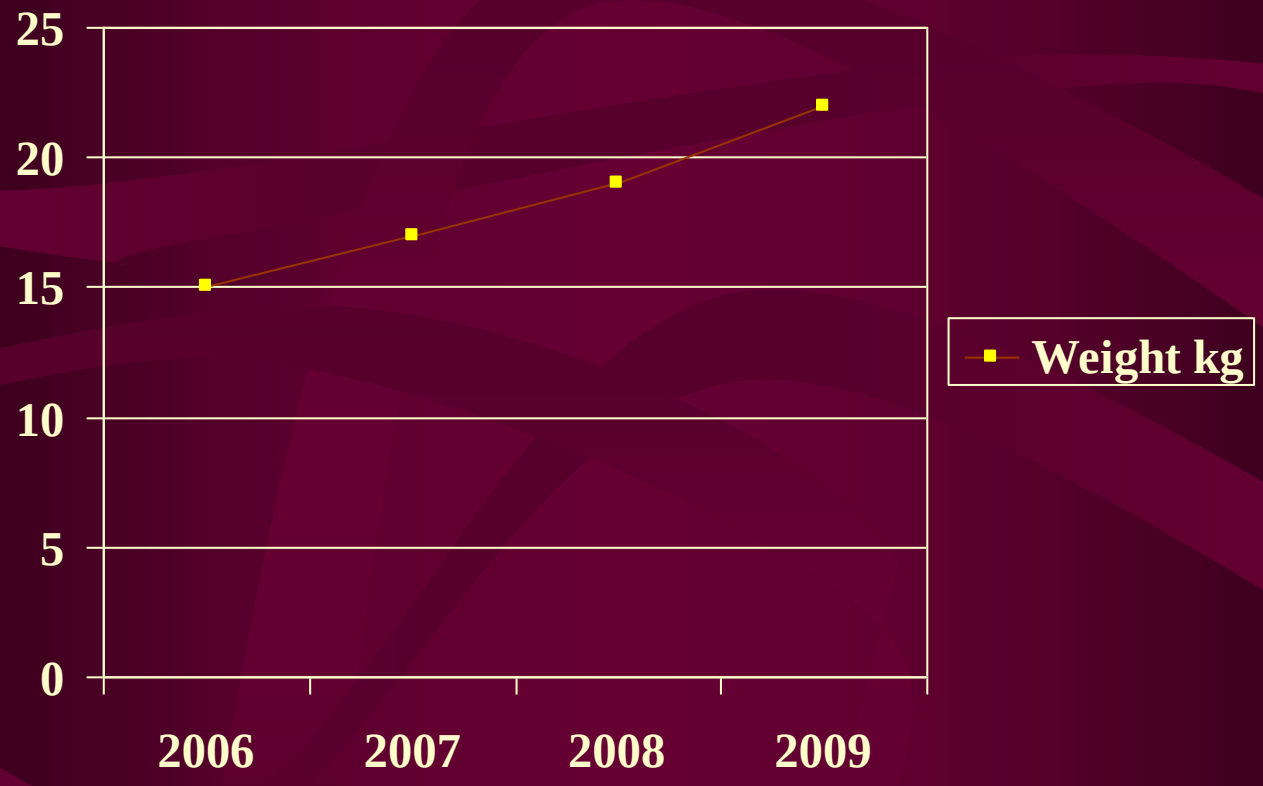

Investigations

- Serum electrolytes, Calcium, Phosphate within normal limits.
- Hemogram,complete blood counts normal.
- Mantoux neg.
- CXR normal.
- ECG, Echocardiogram normal.
- HIV Non Reactive.

Endocrine workup

- ACTH Stimulation test:

  Cortisol Basal - 1.60 mcg/dl.

  1½hrs - 1.50 mcg/dl.

  3 hrs - 1.40 mcg/dl.
- Thyroid profile within normal limits.
- Serum Parathormone – 22.82 pg/ml.(10-169)

Contd..

- Thyroid Antibodies

  Anti microsomal Ab positive.
- Anti Tissue trans glutaminase Ab < 12.3 – normal.
- GAD, ICA negative.

- Type 1 Diabetes.
- Addison’s.
- Thyroid antibodies positive.

AUTOIMMUNE POLYENDOCRINE SYNDROME II

Treatment

- Insulin dosage modified according to SMBG.
- Hydrocortisone and Fludrocortisone supplements.
- Parents have been screened for diabetes, thyroid profile – normal.
- Screening of siblings – Normal thyroid profile.

- The child has been on hydrocortisone and fludrocortisone for the past 8 months, the pigmentation intensity has lessened, but not disappeared.

Discussion

- Type 1 diabetes children - increased risk for other autoimmune diseases such as autoimmune thyroiditis, autoimmune gastritis, Addison‘s, Celiac disease, Vitiligo.

APS - 1

- Genetic locus – chr.21q. AIRE gene.
- Triad – Chronic mucocutaneous candidiasis, Hypoparathyroidism, Adrenal insufficiency.
- Index case – 2 required for diagnosis.
- Sibs – 1 required.
- Lifelong surveillance needed.

APS 2

- 1926 - Schmidt described association between Addison's disease and thyroiditis.
- 1964 – Carpenter included Type 1 DM in this syndrome.
- Most common of the polyglandular syndromes.

APS 2

- Atleast 2 of the following criteria:

  Adrenal insufficiency

  Autoimmune thyroid disease

  Type 1 DM
- Adrenal insufficiency – concurrent or delayed onset for 2 decades or never manifested.
- No identifiable pattern of inheritance.

Comparison

Characteristics	**APS 1**	**APS 2**
Inheritance	Autosomal recessive	Polygenic
Age at onset	Infancy	20 – 40
Gender	Equal	Female preponderance
Genetic association	AIRE gene	HLA assoc

Characteristics	APS 1	APS 2
Addison's	60 –72%	70%
Hypoparathyroid	79 –96%	Rare
Autoimmune thyroiditis	5%	>70%
Type 1 DM	14%	>50%
Prim hypogonadism	60% female 14% male	5%
Hypophysitis	Not reported	Reported

Clinical features	APS 1	APS 2
Pernicious anemia	13%(early)	As common
Chr mucocut candidiasis	100%	Not reported
Vitiligo	13%	5%
Alopecia	29%	Reported
Celiac disease	-	2-3%
Autoimmune hepatitis	12%	Not reported
Myasthenia,Parkinson	Not reported	Reported

Management

- Hormonal replacement remains the only form of treatment of polyglandular syndromes.
- Onset of associated disorders is unpredictable, and are treated as they develop.
- Screening of the individuals and their relatives - prevent morbidity and mortality.

Contd..

- Specific combinations require specific management.
- Thyroid replacement can precipitate life threatening adrenal failure in pts with unrecognised Addison’s.
- Biochemical evidence of hypothyroidism may resolve after glucocorticoid replacement.

Contd..

- Routine thyroid autoantibody screening of all T1DM patients and full endocrine autoantibody testing in those found to be positive is recommended.
- Use of full diagnostic autoantibody panels followed by monitoring of the function of any targeted organ for all Addison's disease probands and their immediate relatives.
- A family history of poly-glandular failure – Red Flag.

Suspect Addison's

- Unexplained recurrent hypoglycemia in T1DM pts
- Reduction in insulin requirement of >15 – 20%
- Development of abnormal pigmentation .
- Decline in growth velocity.
- Family H/O Addison's.

Management of Addison's disease

- Hydrocortisone – mainstay.
- Replace both glucocorticoids and mineralocorticoids.
- Glucocorticoids – To simulate diurnal rhythm, 2/3 dose in morning, 1/3 in late afternoon.
- Side effects – insomnia, irritability, mental excitement.

Contd..

- Other side effects such as hypertension, glycemic control, growth monitoring.
- Complications rare in the doses recommended except for gastritis.
- Stress such as Infections, surgery or trauma - doses of hydrocortisone doubled.

Contd..

- Electrolyte abnormalities – variable, 20 – 30% don’t have hyponatremia or hyperkalemia at any time.
- Complications of mineralocorticoid therapy – hypokalemia, hypertension, even CCF.
- Periodic measurements of body weight, Potassium, blood pressure.

Contd..

- All patients with Adrenal insufficiency, Type 1 Diabetes mellitus should carry medical identity card.

Take Home Message

- High index of suspicion for additional autoimmune disorders in a child with one disease.
- Life long follow up needed .

Acknowledgements

- We thank Dr.Murthy who helped us to perform ACTH stimulation test and for his valuable guidance.


THANK YOU