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.
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

Height (cm)
Growth pattern

![Growth pattern graph showing weight kg from 2006 to 2009.](image)
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.
• 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

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>APS 1</th>
<th>APS 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inheritance</td>
<td>Autosomal recessive</td>
<td>Polygenic</td>
</tr>
<tr>
<td>Age at onset</td>
<td>Infancy</td>
<td>20 – 40</td>
</tr>
<tr>
<td>Gender</td>
<td>Equal</td>
<td>Female preponderance</td>
</tr>
<tr>
<td>Genetic association</td>
<td>AIRE gene</td>
<td>HLA assoc</td>
</tr>
<tr>
<td>Characteristics</td>
<td>APS 1</td>
<td>APS 2</td>
</tr>
<tr>
<td>-------------------------</td>
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<td>---------------</td>
</tr>
<tr>
<td>Addison’s</td>
<td>60 –72%</td>
<td>70%</td>
</tr>
<tr>
<td>Hypoparathyroid</td>
<td>79 –96%</td>
<td>Rare</td>
</tr>
<tr>
<td>Autoimmune thyroiditis</td>
<td>5%</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>Type 1 DM</td>
<td>14%</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Prim hypogonadism</td>
<td>60% female</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>14% male</td>
<td></td>
</tr>
<tr>
<td>Hypophysitis</td>
<td>Not reported</td>
<td>Reported</td>
</tr>
<tr>
<td>Clinical features</td>
<td>APS 1</td>
<td>APS 2</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>---------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>Pernicious anemia</td>
<td>13% (early)</td>
<td>As common</td>
</tr>
<tr>
<td>Chr mucocut candidiasis</td>
<td>100%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Vitiligo</td>
<td>13%</td>
<td>5%</td>
</tr>
<tr>
<td>Alopecia</td>
<td>29%</td>
<td>Reported</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>-</td>
<td>2-3%</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>12%</td>
<td>Not reported</td>
</tr>
<tr>
<td>Myasthenia, Parkinson</td>
<td>Not reported</td>
<td>Reported</td>
</tr>
</tbody>
</table>
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.
• 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