

## Polyglandular Autoimmune Syndrome-Type I

**Rajesh R. Joshi**  
**Sudha Rao**  
**S. S. Prabhu**

*Polyglandular autoimmune syndrome type -I is a rare disorder characterized by mucocutaneous candidiasis (MC), hypoparathyroidism (HP) and adrenal insufficiency, requiring regular follow up as the components of the syndrome appear at different age groups. We report a 6½-year-boy having this syndrome and presenting with MC, HP and ectodermal dystrophy.*

**Key words:** *Candidiasis, Hypopara-thyroidism, Polyglandular,*

### Introduction

Polyglandular autoimmune syndrome type -I (PGA-I) also known as polyendocrinopathy-candidiasis-ectodermaldystrophy (APECED) is a very rare disorder predominantly reported from Finland(1) and Iranian Jews(2). It is a autosomal recessive disease with mutations in the autoimmune regulator gene on chromosome 21q22.3(3) leading to a disorder of immune system with destruction of predominantly endocrine glands, candidiasis (mostly superficial) and ectodermal dystrophies. We report a 6½-year-old boy with PGA-I who had chronic candidiasis, hypoparathyroidism and ectodermal dystrophy.

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*From the Department of Pediatrics, B.J.Wadia Hospital for Children, Parel, Mumbai 400 012.*

*Correspondence to: Dr. R.R. Joshi, D/3, Parshvanath Apartments, Saibaba Nagar, Borivali (West), Mumbai 400 092. E-mail: rrj23@rediffmail.com*

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### Case Report

A 6½-year-old boy born out of non-consanguinity presented with episodes of giddiness and staring spells since 15 days and generalized convulsions since one day.

At 4 years of age he had oral candidiasis lasting for 1½ years which got cured with prolonged fluconazole therapy. Following that he had pitting of nails and yellowish discoloration of tooth. At 5½ years he had loss of scalp hair, eyebrow and eyelashes. He had a male sibling of age 4½ years who was asymptomatic.

On examination he had a weight of 20 kg (25-50th centile) and a height of 114 cm (25th centile and within MPH range). The vital parameters were normal. There was alopecia with only small patch of hair on frontal region, scanty eyelashes and eyebrow. His teeth were yellow and carious and nails showed pitted dystrophy. There was no evidence of mucocutaneous candidiasis. The systemic examination was normal.

Laboratory investigations revealed Hb-11 g/dL with normal RBC indices. PTH was low *i.e.*, less than 5 pg/mL (normal range 9-80) with low ionic calcium of 0.59 mmol/L and low total Ca of 5.6 mg/dL. Serum phosphorus was 5.4 mg/dL and alkaline phosphatase 96 IU/mL. Fasting and post-prandial blood sugar, SGPT, serum proteins, creatinine and electrolytes were normal. Sr cortisol (8 am) at presentation was 19.76 mcg% (N: 4.3-22.4). ACTH stimulation was not done. Thyroid function tests were normal. Antimicrosomal antibodies, ANA and anti-dsDNA were negative. Ophthalmological examination was normal.

He was diagnosed to have PGA-I or APECED based on presence of hypoparathyroidism, ectodermal dystrophy (pitted nail dystrophy and enamel hypoplasia as evident

by yellow tooth) and past history of candidiasis.

He was treated with calcium supplements and calcitriol 0.25 mcg daily. Serum calcium increased with treatment and he was monitored regularly for achieving good calcemic control. He did not have convulsions or giddiness after treatment. Topical minoxidil was applied for alopecia after which there was hair growth. We have a follow up of 2½ years. He has not developed other components of the disease other than mentioned above.

### Discussion

Neufeld, *et al.* in 1980 identified 3 major types of autoimmune polyglandular syndromes(4). Polyglandular autoimmune syndrome type-I is due to a monogenic mutation of AIRE (autoimmune regulator discovered in 1997) which codes for a transcription factor(3). Its pathophysiological substrate seems to be related to an anomaly of normal immunological tolerogenesis leading to the formation of autoantibodies directed against specific tissue antigens: surface receptors, intracellular enzymes, secreted proteins (hormones). The spectrum of PGA-I is broad (5-7). The most frequent components – chronic mucocutaneous candidiasis (MC), hypoparathyroidism (HP) and adrenocortical insufficiency (AI) – usually appear in childhood in order listed with the prevalence of disease components increasing with age. Presence of at least two of the above components is required for clinical diagnosis which was present in our patient (MC and HP).

MC is commonly the first manifestation, the incidence peaking over the first 2 years of life. It affects the angles of mouth or the oral cavity and sometimes causes esophagitis, vulvovaginitis, perianal lesions or intestinal mucosal candidiasis(4,5,7).

Among the endocrinopathies, HP is usually first seen at the age of 2-11 years. HP presents with features of hypocalcemia. AI presents at 4-12 years with deficiency of aldosterone and cortisol which may be dissociated for many years(1,5). Ectodermal dystrophy presents as enamel hypoplasia in three-fourths of patients and as pitted nail dystrophy in half of patients, while alopecia is seen in 4%(1), these features being present in our patient. Less common clinical manifestations are hypergonadotrophic hypogonadism, type-1 diabetes mellitus (DM), autoimmune thyroid disease (AITD), pernicious anemia, chronic atrophic gastritis, chronic active hepatitis, asplenia and keratoconjunctivitis(5,7).

End organ functions are necessary to confirm the diagnosis like ACTH and cortisol for AI; calcium and PTH levels for HP; fungal skin scraping for candidiasis; CBC, MCV and vitamin B<sub>12</sub> levels for pernicious anemia; testosterone/estradiol, FSH and LH as necessary for hypogonadism; T3, T4, TSH for AITD and blood sugar level for DM. Some of these tests may have to be done annually to find out new disease manifestations.

After finding out disease components regular follow up and therapy is required. Follow up should be at least twice yearly(1). In our case more frequent follow up (2-3 monthly) was done as hypoparathyroidism requires a tight monitoring so as to achieve good calcemic control and maintain serum calcium at 8.5-9 mg%, avoiding kidney damage. During follow up development of new disease components should also be monitored. For detecting component diseases search for antibodies predicting new disease components is a valuable diagnostic tool. These antibodies are against CYP450c21, CYP450scc, CYP450c17c (for adrenalitis); CYP450-1A2 (hepatitis); tryptophan hydro-

xylase(intestinal dysfunction); GAD(DM); thyroid peroxidase, thyroglobulin (AITD); and intrinsic factor (parietal cell autoimmunity)(1). These facilities are very limited and costly in India. Search for AIRE mutations is available only in few specialized centres in the world and not in India. Moreover owing to large number of mutations, PGA-I cannot be excluded by routine DNA analysis(3).

Treatment of this disease is that of individual components as was offered to our patient for MC and HP. Other disease components which require therapy are steroid replacement for AI; insulin for DM; immunosuppressive therapy for hepatitis and intestinal dysfunction; vitamin A, steroids for keratoconjunctivitis; appropriate vaccinations and prophylactic antibiotics for splenic atrophy and vitamin B<sub>12</sub> for pernicious anemia. Our patient's family members were informed about disease and potential new components which may appear and to report without delay if symptoms develop suggesting AI, DM, hepatitis, or any other acute severe illness.

The prognosis is variable depending on how organs are affected and the severity of the disease.

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