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A Rare Presentation of Polyglandular Autoimmune Syndrome Type 1

Ajeitha L
Department of Paediatrics, Madras Medical College and Government General Hospital

Abstract

PGA-I, also known as autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) or as Whitaker syndrome is a rare sporadic autosomal recessive disorder.[1,2,3]Two out of the following three major features are required for clinical diagnosis of PGA[1,3]-1.autoimmune adrenal insufficiency 2.hypoparathyroidism 3.mucocutaneous candidiasis Other associated features include gonadal failure, hypothyroidism, type-I diabetes mellitus, dental enamel hypoplasia, ungula dystrophy, tympanic membrane sclerosis, vitiligo, keratopathy, pernicious anaemia, malabsorption, asplenism, achalasia,cholelithiasis, chronic active hepatitis, Sjogrens syndrome,haemolytic anaemia, vasculitis, and hypophysitis [1,2,3] The usual order of manifestation is candidiasis followed by hypoparathyroidism and then addisons.[4] We present a rare presentation of type 1 APS presenting without candidiasis (.In a single case of PGA-I reported by Bhansali and colleagues, no candidiasis was noted in an East Indian boy aged 16 years.[5]) and with Addisons being the first manifestation. Our case had adrenal insufficiency, hypoparathyroidism and bilateral cataracts.No evidence of candidiasis or ectodermal dystrophy was seen highlighting the varied presentation of PGA-1.

Keywords

PGA, adrenal insufficiency, hypoparathyroidism, autoimmune polyglandular

Introduction

PGA-I, also known as autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) or as Whitaker syndrome is a rare sporadic autosomal recessive disorder.[1,2,3]. Two out of the following three major features are required for clinical diagnosis of PGA[1,3]-1.autoimmune adrenal insufficiency2.hypoparathyroidism3.mucocutaneous candidiasis. Other associated features include gonadal failure, hypothyroidism, type-I diabetes mellitus,dental enamel hypoplasia, ungual dystrophy, tympanic membrane sclerosis, vitiligo, keratopathy, pernicious anaemia, malabsorption, asplenism, achalasia, cholelithiasis, chronic active hepatitis, Sjogrens syndrome, haemolytic anaemia, vasculitis, and hypophysitis[1,2,3]. The usual order of manifestation is candidiasis followed by hypoparathyroidism and then addisons.[4] We present a rare presentation of type 1 APS presenting without candidiasis (In a single case of PGA-I reported by Bhansali and colleagues, no candidiasis was noted in an East Indian boy aged 16 years.[5]) and with Addisons being the first manifestation. Our case had adrenal insufficiency, hypoparathyroidism and bilateral cataracts.No evidence of candidiasis or ectodermal dystrophy was seen highlighting the varied presentation of PGA-1.

Case Report

An 8 year old boy, second born of fourth degree consanguinous parents was apparently normal till five months earlier when he developed lethargy, giddiness on standing and increasing pigmentation of entire body. He did not have anorexia, vomiting, seizures or altered sensorium. He did not have salt craving, fever or myalgia. No sudden deaths in his family. Elder brother was healthy. He did not have history of contact with tuberculosis. On examination ,generalized hyperpigmentation was seen more notably in skin creases. He had orthosatic hypotension. Hair, dentition was normal. There was no evidence of cutaneous candidiasis. Systemic examination was normal. On evaluation he had hyponatremia, hyperkalemia, low serum cortisol and elevatd ACTH. Serum proteins, urea, creatinine was normal. Ultrasound abdomen was normal. Diagnosis of Addison's disease was made.Work up for other endocrine dysfunction was done. Fasting and post prandial blood sugar, thyroid function test, prolactin, FSH, LH, testosterone, serum calcium, phosphorus was normal. He was started on hydrocortisone and fludrocortisone and advised follow up.

He was re admitted with generalized seizures. On examination had carpopedal spasm. Chovstek sign positive. Serum calcium was 6 mg/dl. serum phosphorus, SGPT were normal,. Serum Parathormone was markedly reduced (1pg/ml. normal 12-72 pg/ml). CT brain was normal. He was managed with intravenous calcium gluconate. Symptoms subsided. Based on the findings of adrenal insufficiency and hypoparathyroidism – two of three criteria being met -a diagnosis of polyglandular autoimmune syndrome type 1 was made. Our case did not have ectodermal findings or candidiasis. Further he developed bilateral cataract, was operated and Intra ocular lens implantation was done. Our case highlights the need to thoroughly evaluate all cases of addison's for other endocrine dysfunction and closely follow up

as the presentation of PGA-1 is varied and associated features may be lacking. Our patient is now on steroids and calcium, his pigmentation has decreased and is on regular follow up.

Initial Hyperpigmentation

Improvement after Oral Steroids

Discussion

Polyglandular autoimmune syndrome type-I(PGA-I) also known as polyendocrinopathy -candidiasis ectodermal Dystrophy (APECED) is a very rare disorder predominantly reported from Finland and Iranian Jews. 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.

Historically, candidiasis was the initial major manifestation to appear, which is true with most of the previous series. Candidiasis is usually the first manifestation to appear1-, usually before the age of 5 years, occurring in 73-100%of all cases. Our case did not have any evidence of candidiasis at all The reason for marked susceptibility to mucocutaneous candidiasis without systemic involvement is unknown. This is followed by hypoparathyroidism usually before 10 years and later by adrenal insufficiency before 15 years of age. Our case had adrenal insufficiency as initial presentation followed by hypoparathyroidism. Our case an additional finding of bilateral cataract which is very rare. 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 B12 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.

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 hydroxylase (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.

Treatment of this disease is that of individual components as was offered to our patient for adrenal insufficiency and hypoparathyroidism. Other disease components which require therapy are ; insulin for DM; immunosuppressive therapy for hepatitis and intestinal dysfunction; vitamin A, steroids for kerato conjunctivitis; appropriate vaccinations and prophylactic antibiotics for splenic atrophy and vitamin B12 for pernicious anemia.

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

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