

A Case of Polyglandular Autoimmune Syndrome Type I with Unusual Presentation

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ABSTRACT

Eight years old girl presented with mucocutaneous candidiasis, nail dystrophy, twitching left half of face, progressively increasing generalized skin hyperpigmentation and hypopigmented patches over both shins. Her investigations revealed low intact PTH level, low serum cortisol, high ACTH, impaired glucose tolerance test and candidal onychomycosis. She was diagnosed as Polyglandular Autoimmune Syndrome (PGA) type I. She also developed idiopathic generalized epileptiform seizures and *Alcaligenes faecalis* septicemia not previously reported with PGA type I. The patient responded well to alphacalcidol, hydrocortisone, valproate sodium, topical antifungal and systemic antibiotics.

Key words: Polyglandular Autoimmune Syndrome type I. Seizures. Autoimmune. Hypocalcaemia. *Alcaligenes faecalis* septicemia.

INTRODUCTION

Polyglandular autoimmune syndrome type I (PGA-I) is an extremely rare condition with incidence of less than 1 in 100,000.¹ Clustered cases have been reported in certain homogeneous ethnic populations. Iranian Jews, Sardinians, and Finns have reported frequency as high as 1:9000.² Male to female ratio of 0.8 to 2.4 has been reported with slight female preponderance.³ It is sporadic autosomal recessive condition with genetic locus localized on band 21p22.3 causing mutation of AIRE (Autoimmune regulator) gene.⁴ Candidiasis is usually the first clinical manifestation to appear, usually before the age of 5 years, followed by hypoparathyroidism (usually before 10 years of age), and Addison's disease (usually before 15 years).²

In this case report, we present a case of polyglandular autoimmune syndrome type 1 (PGA-I) with some unusual presentation.

CASE REPORT

An 8 years old girl, resident of rural North Eastern Punjab, Pakistan, presented with complaint of progressively increasing episodes of twitching over left half of face for last 2 weeks, becoming almost persistent for last 2 days (Figure 1). These movements were not associated with any behavioral disturbance, altered conscious level or cramps.

Two years ago, she started to develop distortion of nails of both hands and feet, starting from nail margins, gradually involving whole nail (Figure 2). There was a repeated occurrence of whitish lesions on her tongue, limiting her oral intake. She started to develop hypopigmented patches over both shins gradually increasing in dimensions (Figure 3). About 6 months ago, the parent also noticed that her complexion was getting darker. Two months ago, she suffered an episode of generalized tonic clonic seizure associated with uprolling of eyes for 3 minutes and urinary incontinence followed by a brief period of postictal drowsiness. She recovered without any neurological deficit. She was a developmentally normal school going, vaccinated girl with related parents and without history of previous hospitalization or history of similar complaint in any other family member.

She was a thin built child with height and weight at 3rd centile on growth chart for her age with continuous twitching of left half of face. She had a pulse rate of 116/min, respiratory rate 22/min and BP 75/55. She had dystrophic nails, vitiligo patches over shins trunk and face. There was generalized increased pigmentation, particularly of oral mucosa and palmer creases. Chvostek's sign was positive. Rest of systemic examination was unremarkable.

Her investigations revealed low serum calcium (6.7 mg/dL, normal: 8.8–11.0 mg/dL), upper normal level of phosphate (4.4 mg/dL, normal: 2.4–4.5 mg/dL), normal alkaline phosphatase 113 U/L, low serum sodium (131 mEq/L, normal: 135–154 mEq/L), high serum potassium (6.5 mEq/L, normal: 3.5–5.4 mEq/L), normal random blood sugar 123 mg/dL and compensated metabolic acidosis (pH 7.40, HCO₃ 10.1 mmol/L, base deficit 11.5 mmol/L). Further investigation revealed low intact PTH level (10.7 pg/mL, normal: 11–67 pg/mL), low serum cortisol (8A.M. sample 1.1 µg/dL, normal: 5–23 µg/dL),

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Received September 29, 2009; accepted January 7, 2011.



Figure 1: Eight years old girl showing increased pigmentation, hypopigmented lesion below lower lip and twitching left half of face.



Figure 2: Dystrophic nails of hand.



Figure 3: Hypopigmented vitiligo lesions over both shins.

high ACTH (78 pg/mL, normal: < 46 pg/mL) and impaired glucose tolerance test (fasting 112 mg/dL, 2 hours 144 mg/dL). Nail scrapings confirmed candidal onychomycosis. No autoantibodies could be tested for due to unavailability of facilities.

On the basis of clinical findings and investigations, she was diagnosed a case of polyglandular autoimmune syndrome type I. She was started on intravenous calcium gluconate, alphacalcidol and hydrocortisone with adequate hydration. Her blood pressure improved along with normalization of electrolytes within 48 hours. Twitching improved on the third day of treatment although normalization of serum calcium levels took 6 days. Candidiasis responded to oral fluconazole. Clobetasol ointment (0.5%) was applied for vitiligo lesions. On the 5th day of treatment, she acquired nosocomial *Alcaligenes faecalis* septicemia with fever, generalized maculopapular rash, an abrupt rise in WBC to $21.4 \times 10^9/L$ with 83% neutrophils and elevated CRP (48 mg/L). She responded to intravenous antibiotics within 48 hours. She developed multiple episodes of generalized tonic clonic seizure on 7th admission day and eventually status epilepticus continuing for 40 minutes despite normal ionized calcium and magnesium levels.

Her CSF examination and MRI scan of brain were normal. EEG showed multifocal and generalized epileptiform activity with slow background. Seizures being unresponsive to calcium, anti-convulsants were considered. The seizure subsided with loading dose of phenytoin followed by valproate sodium. She recovered without any neurological sequelae. Valproate sodium was discontinued after 6 months of seizure-free interval. Mucocutaneous candidiasis resolved with one exacerbation at 4 months follow-up, requiring topical antifungal. At one year follow-up, she is still on alphacalcidol, calcium supplement and hydrocortisone with improvement in her general health, growth parameters and complexion, and normalization of calcium and ACTH levels. Vitiligo remained static and Ultra violet light B (UVB133) treatment is planned.

DISCUSSION

Polyglandular autoimmune syndrome (PGA) was first recognized in 1929 by Thorpe and Handley as an association of mucocutaneous candidiasis with adrenal failure. The pathogenesis involves formation of auto-antibodies directed against cell surface receptors, intracellular enzymes and secreted proteins mainly hormones.⁵ Other manifestations include diabetes mellitus type 1, vitiligo, alopecia, hypogonadism, pernicious anemia hypothyroidism and malabsorption.⁶ Rarely reported manifestations include severe airway obstruction and pulmonary involvement.⁷ The condition is extremely rare with worldwide prevalence of 1:10000. Ethnic clusters have been reported mostly in Iranian jews and homogenous ethnic European populations probably due to consanguineous marriages and/or clustering of descendants of common family founders.² This case is the first reported from Punjab, Pakistan. Gender distribution vary among various reports from 0.8 to as high as 2.4 female preponderance.² However, considering the small number of reported cases, this deduction may not be accurate.

The first manifestation usually occurs by the 5th year of life and complete evolution of the three main diseases takes place before the third decade of life. Accompanying diseases continue to appear until at least the fifth decade.³ In the majority of cases, candidiasis is the first clinical manifestation to appearing before the age of 5 years. It is followed by hypoparathyroidism occurring before the age of 10 years and adrenal failure before 15 years of age. This case showed the same sequence of major manifestations at characteristic ages.

T-cell defect has been documented in PGA-I resulting in localized candidiasis however, systemic susceptibility has not been documented.⁸ Mucocutaneous candidiasis in this case developed at 6 years recurring despite treatment but did not suffer systemic candidiasis consistent with previously reported cases. On the other hand, this patient developed *Alcaligenes faecalis* septicemia, a low virulence organism prevalent in fruit juices and

food preservatives. Such fulminant nosocomial infection due to low virulence organism contracted by this patient was probably associated with immune deficient state. However, such systemic infection has not been reported previously.

Idiopathic epileptiform seizures in this patient have been rarely reported previously. Carpopedal spasm and hypocalcaemic seizures are the most common presentations secondary to hypoparathyroidism in late childhood and adult life. Other symptoms reported previously include laryngospasm, leg cramps, cataract, papilledema and diffuse non-specific encephalopathy.⁶ In this patient, normal ionized serum calcium levels and EEG did not support hypocalcaemic origin of seizures. Septicemia had already settled by the time she seized and MRI did not show any microinfarcts or microcalcifications. Hence we labeled them idiopathic epileptiform in nature. Such epileptiform seizures requiring anticonvulsant therapy have rarely been reported earlier with PGA-I.

Adrenal crisis is one of the most serious manifestations of PGA-I. This case had signs and symptoms of both glucocorticoid and mineralocorticoid deficiency though never suffered adrenal crisis. She responded well to hydrocortisone. Type 1 DM is five times more common in these patients than general population.⁹ This case did not develop DM, however, glucose tolerance test was consistently impaired during 1 year follow-up. Close monitoring was continued without any active intervention.

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