A rare association of polyglandular autoimmune endocrinopathy type II with hypoparathyroidism

Manish Gutch, Sukriti Kumar, Syed Mohd Razi, Sanjay Saran, Keshav Kumar Gupta

ABSTRACT

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Case Report: A previously diagnosed primary hypothyroid 35-year-old female admitted with a 15-day history of general malaise. She complained of polyuria, polydipsia, weight loss, abdominal pain and vomiting. She was diagnosed diabetic ketoacidosis due to previously undiagnosed type I diabetes (capillary blood glucose >500mg/dL, pH 7.20) and intravenous fluids and intravenous insulin infusion was started. After four hours, despite of appropriate fluid resuscitation and normalization of blood glucose, her condition had deteriorated, she became more tachycardic and hypotensive. At this time, the patient was reassessed and a short Synacthen test was carried out then hydrocortisone was administered immediately after the short Synacthen test. Test result showed hypocortisolemia (Addison's disease). During the course of hospital stay she developed tetany then on further investigations hypoparathyroidism was also diagnosed. Herein, we report a rare case of report Ppolyglandular autoimmune endocrinopathies type II with simultaneous involvement of parathyroid gland.

Conclusion: Patients presented with an autoimmune disease should be screen for other autoimmune conditions as early detection of other organs specific autoantibody may reduce morbidity and mortality associated in patients with autoimmune polyglandular syndrome.

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CASE REPORT

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Keywords: Type II polyglandular autoimmune syndrome, Diabetes, Schmidt's syndrome, Addison's disease, Hypothyroidism, Hypoparathyroidism

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INTRODUCTION

Polyglandular autoimmune syndrome type II (PGA type II) is a very uncommon endocrine condition characterized by one or more organ specific autoantibodies directed against specific antigen which occurs with a frequency of 1.4–2.0/100, 000 in general population. Females are affected more commonly than males. Various other endocrine organs are involved beside adrenal (adrenal insufficiency), pancreas (T1DM), and thyroid (hypothyroidism), these are gastric parietal cells (pernicious anemia), melanocytes (vitiligo), other

less common associations are hypergonadotropic hypogonadism, chronic autoimmune hepatitis, coeliac disease, autoimmune diabetes insipidus and rarely lymphocytic hypophysitis, stiff-person syndrome and myasthenia gravis [1]. T1DM is the first presentation in about 60% of patients; while adrenal insufficiency is the first presentation in about 30% of cases and both present simultaneously in 8–10% of cases. Carpenter noticed the association of Schmidt's syndrome (Addison's disease and hypothyroidism) and diabetes mellitus in his case review in 1964, in this review, 20% of Schmidt's syndrome cases also had diabetes mellitus and the triad is sometimes referred to as Carpenter's syndrome [1]. The separate disorders usually present over a number of years. Here a very unusual association of PGA type II with hypoparathyroidism is seen and it highlights the importance of checking parathyroid function while dealing with constellation of endocrine disorders.

CASE REPORT

A 35-year-old female presented at emergency with a 15-day history of malaise, tiredness and feeling faint. She had also noticed increased thirst, drinking more than 3L/day, urinary frequency, leg cramps and reduced exercise tolerance. For the preceding week, she had been troubled by nausea and vomiting to the extent that she was unable to eat but had been able to drink. The day prior to admission, she had developed abdominal pain. She was a non-smoker and non-drinker housewife.

On examination, she was a bit obese, dehydrated and anxious. Her temperature was 96.8°F, pulse 120/minute and blood pressure 50 mmHg systolic. Cardiovascular and respiratory examination were normal and her abdomen was soft but tender to light palpation with normal bowel sounds and no rebound or guarding. A capillary blood glucose was >500 mg/dL. Arterial blood gases were normal (pH 7.20, pCO₂ 36 mmHg, pO₂ 87 mmHg, BE -2.6 mmol/L, HCO₃ -11.8). Urine dipstick was positive for ketones (+++) and glucose (+++).

After the initial assessment the impression was that the patient was newly diagnosed diabetes and had developed diabetic ketoacidosis (DKA), she was dehydrated and her abdominal symptoms may have been related to her diabetes but a polyendocrine syndrome should be considered. She was treated with standard protocol for DKA (Normal saline and Regular Insulin drip) and broad spectrum antibiotics (ceftriaxone and metronidazole). Routine investigations (glucose, urea, creatinine, electrolytes, calcium and liver function), and serum amylase were carried out (Table 1).

The patient was reviewed four hours later. At this time despite her glucose normalizing and fluid resuscitation having occurred her pulse had increased and her blood pressure had not improved (Table 1). She looked worse and did not feel any better despite appropriate treatment. Base line serum cortisol and thyroid function tests, and a short

Synacthen test were carried out then hydrocortisone 100 mg was started immediately. Her pulse became palpable and blood pressure gets improved. Thyroid stimulating hormone (TSH) 8.34 uIU/mL (normal range 0.4–5.0), antithyroid peroxidase 5077.1 IU/mL (normal range 60), free thyroxine 0.8 ng/dL (normal range 0.7–2.0 mg/dL), the patient had been taking levothyroxine 100 µg/day for the past 4 years, and we made her continue that as such.

During second day of hospital stay patient suddenly developed tetany and immediate serum calcium and PTH samples was withdrawn and patient put on intravenous calcium infusion (37.5 mg elemental calcium per hour in 5% dextrose). Patient tetany improved after two hours of calcium infusion. Subsequent result revealed low serum calcium (total-6.6 mg/dL and ionic 3.4 mg/dL) and PTH level was 4.67 pg/mL (normal range 8–51 pg/mL) and her protein and albumin were 6.6 g/dL (normal range 6.7–8.8 g/dL) and 3.8 g/dL (normal range 3.5–5.5g/dL) respectively, while serum magnesium was 2.1 mg/dL. General condition of the patient was improving till day 4. On day 5, the patient developed severe breathlessness, restlessness, along with right sided pleuritic chest pain, and found to have developed type 1 respiratory failure then she was immediately intubated and puts on mechanical ventilator but patient expired on day 5 of admission due to cardiorespiratory arrest.

DISCUSSION

Autoimmune hypoparathyroidism is present in 80–85% of patients with autoimmune polyendocrine syndrome type I and in up to 5% of patients with autoimmune polyendocrine syndrome type II. The autoantigens were unknown until the extracellular domain of the calcium-sensing receptor was identified as a potential target. Thus, it has been found that calcium-sensing receptor autoantibodies are relevant markers of autoimmune hypoparathyroidism [2].

Patient's relatives of PGA II found to have increasing tendency towards other autoimmune condition [1]. Human leukocyte antigens (HLA) region II (i.e., major histocompatibility complex) is most commonly associated with PGA II and that too mainly with HLA haplotypes DR3 (DQB*0201) and DR4 (DQB1*0302) regions [3].

Various types of organ specific antibodies can be found in patients with PGA II these are 21 hydroxylase autoantibodies (21OHAb) directed against adrenal cortex, thyroperoxidase (TPOAb), thyroglobulin (TGAb) and TSH receptor autoantibodies (TRAb) directed against thyroid; insulin (IAA), and glutamic acid decarboxylase autoantibodies (GADAb) directed against the endocrine pancreas [4].

Our patient was a previously known case of hypothyroidism admitted with symptoms of DKA and undiagnosed T1DM which get unveiled here. She was treated appropriately for DKA but in the mean time she was also found to have hypotension that was not

Table 1: Laboratory investigations and vital parameters during course of her hospital stay

Date Parameters (reference ranges)		August 2011				
		11	12	13	14	15
Hematocrit (35–44% for female)		44.3		42.6	40.1	35.3
Total WBC count (4000–11500 cells/mm ³)		12,600			16,200	11,300
Platelet count (1.5–4.5 lacs/mm ³)		1.75		1.45	1.67	1.60
Random blood sugar (mg/dL)		530	426	356	300	275
Serum sodium (135–148 meq/L)		128	126	122	128	130
Serum potassium (3.5–5 meq/L)		5.6	5.0	4.3	4.2	4.0
Serum urea (15–43 mg/dL)		68			60	
Serum creatinine (0.6–1.2 mg/dL)		1.54			1.78	
Urinary ketones		++++	+++	++	+	---
Fluid given (litres in 24 hours)		7	5.5	4.0	3.5	3.0
Temperature (°F)		96.8	98.8	99.2	97.4	102.0
Blood pressure (mmHg)		50*	100/48	110/46	94/40	70/40
Respiratory rate (per minute)		24	22	26	36	48
Pulse rate (per minute)		120	116	114	104	150
Serum calcium (mg/dL)	Total		6.6		7.8	
	Ionic		3.4		4.1	
Serum PTH (15–65 pg/ml)			4.70			
ABG	PO ₂ (80–100 mmHg)	87	92	90	86	38
	PCO ₂ (35–45 mmHg)	36	40	42	38	49
	HCO ₃ (20–24 mmol/L)	11.8	13.2	14.2	14.7	14.6
	pH (7.35–7.45)	7.20	7.26	7.30	7.33	7.10

*systolic blood pressure

responding to intravenous fluid which was initially suspected to be due to hypocortisolemia. Later on investigations as well as response of blood pressure to hydrocortisone confirmed the Addison's disease.

When considering a diagnosis of Addison's disease in the acute situation it is useful to remember that a short Synacthen test can be done at any time of day and that a 30-minute cortisol level has diagnostic significance. Measuring the ACTH before giving the Synacthen and any steroids also confirmed primary adrenal failure. Although a rare situation, Addison's disease does co-present with diabetes and fortunately in this situation the lack of response to appropriate treatment triggered the review of the patient and the diagnosis was established.

When further investigating this group of patients, it is important to remember that glucocorticoid deficiency through feedback mechanisms causes an increase in TSH so minor elevations in TSH may not be due to hypothyroidism and should be monitored for improvement with treatment of the Addison's disease. Although uncommon, this case provides a useful reminder of the clustering of endocrinopathies that can occur and that it is important to screen for them on presentation and at follow-up.

Polyglandular autoimmune can present with varied

forms general rule is to give cortisol replacement first then thyroxine and others. If patient of PGA syndrome presents with primary hypogonadism, appropriate hormone replacement therapy should be given in the form of testosterone or HRT. If patient presents with celiac disease, gluten free diet is advisable.

CONCLUSION

This case highlights the importance that, if a patient fails to respond to appropriate treatment for their uncontrolled T1DM or its acute complications, other possible endocrine abnormalities should also be considered besides known factor such as sepsis.

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Author Contributions

Manish Gutch – Substantial contributions to conception and design, Acquisition of data, Analysis

and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Sukriti Kumar – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Syed Mohd Razi – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Sanjay Saran – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

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Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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