Polyglandular autoimmune syndrome type 2: diagnosed in the intensive care unit

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Introduction

Polyglandular autoimmune syndrome type 2 is a rare syndrome that commonly has the constellation of three diseases: diabetes mellitus type 1, hypothyroidism and adrenal insufficiency. Owing to the diabetes mellitus type 1, patients require life-long insulin therapy and blood glucose levels need to be monitored. They are at risk for chronic complications of diabetes such as neuropathy, nephropathy and retinopathy. More acutely, due to fluctuations in blood glucose levels, they are at risk for hypoglycemia with neuroglycopenic symptoms and ketoacidosis. Hypothyroidism is diagnosed by measuring the thyroid hormone levels and if inappropriately low is treated with replacement therapy. Patients with adrenal insufficiency experience symptoms due to low glucocorticoid and mineralocorticoid levels in the body, due to decreased or absent production. We present a case in which a patient presented with a picture of diabetic ketoacidosis was found to have hypothyroidism in her medical history and was diagnosed with adrenal insufficiency in the intensive care unit (ICU), later confirmed as an outpatient to be permanent. Based on the three diagnoses it was concluded that she has polyglandular autoimmune syndrome type 2.

Case report

Emergency department course

A 36-year-old woman of Chinese descent was brought to the Emergency Department (ED) by her colleagues after being found unresponsive at her apartment. Per account she failed to report to work for 2 days and when her colleagues went to check up on her, they found her in her current state. Her past medical and other histories were limited at the time. In the ED the patient was in altered mental status, responsive only to pain and loud verbal stimuli. Neurological examination was difficult due to her current state but her

reflexes were delayed; other physical examination was benign.

Her vital signs and laboratory analysis in the ED were concerning and the ICU was consulted (Tables 1 and 2). The results of her laboratory analysis were consistent with a picture of diabetic ketoacidosis (Tables 3, 4 and 5). She was immediately transferred to the ICU setting and started on a diabetic ketoacidosis protocol with fluids, insulin drip, electrolyte replacement, warming blankets for hypothermia and bilevel positive airway pressure for support.

ICU course

After 18 hours in the ICU her anion gap finally closed and her blood glucose levels normalized, although her vitals failed to improve and resembled admission values. During this time her colleagues brought in her home medications which included subcutaneous insulin as well as levothyroxine for hypothyroidism. Equipped with this new information her thyroid hormone levels were measured and were consistent with hypothyroidism (Table 6). Her random cortisol level was checked, which revealed a low value, considering her current stressful state.

Based on this new information the patient was started on levothyroxine for severe hypothyroidism. Furthermore, owing to the concerns regarding adrenal crisis, the patient was also started on dexamethasone as well as fludrocortisone. Additional investigation for low cortisol levels was done by performing a cosyntropin-stimulation test, which revealed a subnormal value of cortisol (Table 7).

Table 1. Vital signs on admission.

Temperature	31°C	Hypothermic
Blood pressure	70/42 mmHg	Hypotensive
Heart rate	40 bpm	Bradycardic
Respiratory rate	8–10/minute	Bradypnic

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Table 2. Arterial blood gas.

Arterial blood gas	pH = 6.91 (7.35–7.45)	PCO ₂ = 9.58 (4.7–5.9 kPa)	PaO ₂ = 12.24 (11–13 kPa)	HCO ₃ = 9 (21–28 mmol/l)
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Table 3. Complete blood count.

Complete blood count	Differential
Hemoglobin = 9.6 (Female: 12.0–16.0 g/dl)	Neutrophils = 73% (54–62%)
Hematocrit = 29.1 (Female: 36–46%)	Lymphocytes = 8% (25–33%)
Platelets = 167 (150,000–400,000/mm ³)	Monocytes = 5% (3–7%)
Leukocytes = 28.2 (4500–11,000/mm ³)	Eosinophils = 12% (1–3%) high
	Basophils = 2% (0–0.75%)

Table 4. Basic chemistry.

Basic chemistry	Reference values
Sodium = 122 mEq/l	135–145 mEq/l
Potassium = 3.9 mEq/l	3.5–5.0 mEq/l
Chloride = 84 mEq/l	95–105 mEq/l
Bicarbonate = 9 mEq/l	22–28 mEq/l
Blood Urea Nitrogen = 4.64 mmol/l	2.9–8.2 mmol/l
Creatinine = 61.88 µmol/l	53–106 µmol/l
Serum Glucose = 40.74 mmol/l	3.9–6.1 mmol/l
Calcium = 1.95 mmol/l	2.05–2.55 mmol/l
Magnesium = 0.85 mmol/l	0.65–1.05 mmol/l
Phosphorus = 0.45 mg/dl	0.74–1.52 mmol/l

fluids and antioxidants. She reported that her insulin requirement during this time increased and she slowly felt weaker until she went to bed and was found by her colleagues 2 days later.

Prior to transfer out of the ICU, the patient was told of the new diagnosis by an endocrinologist. She was told that she may have polyglandular autoimmune syndrome type 2 and that, in addition to her insulin and levothyroxine, she will need to be on dexamethasone as well as fludrocortisone for her adrenal insufficiency; as replacing dexamethasone with hydrocortisone can alter cosyntropin test results, repeat tests were planned to be performed as an outpatient.

Table 5. Urinalysis.

Urinalysis	Glucose 3+	Ketones positive	Trace protein
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Hence, it was concluded that the patient had adrenal insufficiency. Due to her current illness it was unclear whether it was relative or primary insufficiency.

Hospital course

After spending 5 days in the ICU the patient's condition improved and prior to transfer to the medical floor further history was obtained. The patient reported that she was diagnosed with diabetes mellitus type 1 at the age of eight and since then has been taking insulin subcutaneously as prescribed. She stated that she was diagnosed with hypothyroidism in her teenage years after she suffered amenorrhea with normal secondary sexual characteristics. For the past few days the patient reported to have been suffering from flu symptoms that she was treating at home with

Outpatient office visit

During a subsequent outpatient visit 2 months later, the patient reported feeling better with resolution of all of her symptoms. She reported a normal appetite and diet with some weight gain attributed to steroids. A repeat cosyntropin test result yielded a cortisol value of less than 11 (<18 µg/dl diagnostic). She was switched to hydrocortisone as a life-long adrenal replacement therapy.

Discussion

Polyglandular autoimmune syndrome type 2 entails a group of several disorders involving the endocrine glands. Several endocrine glands can be involved and as the name suggests, via autoimmune mechanisms. Polyglandular autoimmune syndrome type 2 is a rare condition and the diagnosis is not made at once and requires several years as the syndrome itself takes several years to develop in patients. More commonly patients have autoimmune adrenal insufficiency (100%), autoimmune thyroid disease (69–82%) and diabetes mellitus type 1 (30–52%). Other

Table 6. Thyroid hormone levels and random cortisol level.

Thyroid-stimulating hormone = 12 [0.4–4.2 mIU/l]	Thyroxine (T₄ total) = 47.86 [206–309 nmol/l]	Random cortisol level = 193.12 [140–690 nmol/l]
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Table 7. Cosyntropin stimulation test.

Cosyntropin test result loading = 250 µg	Baseline = 7 µg	After 60 minutes = 12 µg (< 18 µg/dl diagnostic)
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autoimmune conditions include vitiligo (4.5–11%), chronic atrophic gastritis, with or without pernicious anemia (4.5–11%), hypergonadotropic hypogonadism (4–9%), chronic autoimmune hepatitis (4%), alopecia (1–4%), hypophysitis ($< 1\%$), myasthenia gravis ($< 1\%$), rheumatoid arthritis ($< 1\%$), Sjögren's syndrome ($< 1\%$) and thrombocytic purpura ($< 1\%$) [Betterle *et al.* 2002].

Adrenal insufficiency is the most common disease in the syndrome but may not present first, as was the case with our patient. Patients may present and be diagnosed with other diseases such as diabetes and thyroid disorders, but finally based on incidence reports the adrenal system is affected. As the adrenal system is affected the patients can present with fatigue, weakness, anorexia, nausea, vomiting, abdominal pain, salt craving, diarrhea, constipation and syncope [Majeroni and Patel, 2007]. Common signs include weight loss, cutaneous and mucosal pigmentation, hypotension and hypoglycemia. Laboratory evaluation is notable for decreased sodium, bicarbonate and chloride levels; decreased basal levels of cortisol, no increase after adrenocorticotrophic hormone (ACTH) or cosyntropin (Cortrosyn) administration; decreased basal levels of aldosterone; increased potassium level; and elevated ACTH levels in primary adrenal insufficiency [Majeroni and Patel, 2007].

Polyglandular autoimmune syndrome type 2 typically occurs in early adulthood with a peak onset during the third or fourth decades and is three times more common in women than in men [Yersal *et al.* 2005]. Polyglandular autoimmune syndrome type 2 can potentially complicate pregnancy due to essential thyroid and adrenal hormone abnormalities [Krysiak and Okopien', 2013]. A methodical approach is warranted. Other types of polyglandular autoimmune syndromes include types 1 and 3 but are not relevant to our case or our discussion as they affect different demographics

Lessons learned

The diagnosis of polyglandular autoimmune syndrome type 2 can be a challenge and the knowledge of and ability to recognize the constellation of diseases takes precedence. A keen eye of the clinician and a good literature search source can assist a primary care physician in arriving at the conclusion with better treatment outcome. In our case, the patient's adrenal insufficiency could have been potentially due to her critical illness in the ICU, but after her recovery, another cosyntropin stimulation test, performed as an outpatient, confirmed the diagnosis of adrenal insufficiency. Dexamethasone is an appropriate glucocorticoid to be used pending a cosyntropin-stimulation test as there is no cross-reactivity compared with hydrocortisone use. Furthermore, she also had significant eosinophilia highly suggestive of primary adrenal insufficiency also individually known as Addison's Disease.

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Conflicts of interest

The authors declare no conflicts of interest in preparing this article.

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