Isolated Adrenocorticotrophic Hormone Deficiency and Primary Hypothyroidism in a Patient Undergoing Long-Term Hemodialysis: A Case Report and Literature Review

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 **Nobumasa Ohara**
BD 1,2 **Michi Kobayashi**
BD 3 **Masafumi Tsuchida**
BD 3 **Ryo Koda**
C 4 **Yuichiro Yoneoka**
CD 3 **Noriaki Iino**

1 Department of Endocrinology and Metabolism, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minamiuonuma, Niigata, Japan
2 Department of Diabetes, Endocrinology and Metabolism, Center Hospital of the National Center for Global Health and Medicine, Tokyo, Japan
3 Department of Nephrology, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minamiuonuma, Niigata, Japan
4 Department of Neurosurgery, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minamiuonuma, Niigata, Japan

Corresponding Author: Nobumasa Ohara, e-mail: oharan@med.niigata-u.ac.jp
Conflict of interest: None declared

Patient: Male, 84-year-old
Final Diagnosis: Isolated adrenocorticotrophic hormone deficiency
Symptoms: Anorexia • fatigue • lethargy
Medication: —
Clinical Procedure: Dynamic endocrine testing • magnetic resonance imaging
Specialty: Endocrinology and metabolic

Objective: Rare co-existence of disease or pathology
Background: Patients with end-stage renal disease undergoing long-term maintenance hemodialysis are more likely than the general population to exhibit primary hypothyroidism. Only a few cases of isolated adrenocorticotrophic hormone deficiency (IAD) among hemodialysis patients have been reported. We herein report an unusual case of a patient undergoing long-term hemodialysis who exhibited both IAD and primary hypothyroidism.
Case Report: A 82-year-old male with end-stage renal disease secondary to immunoglobulin A nephropathy, undergoing hemodialysis for 20 years, was found to have primary hypothyroidism without obvious symptoms and consequently began thyroid hormone replacement therapy with oral levothyroxine. At 84 years of age, he developed anorexia, fatigue, and lethargy. A systemic workup using computed tomography and gastrointestinal endoscopy detected no abnormalities. He did not exhibit electrolyte imbalances, such as hyponatremia or hyperkalemia, and had normal morning blood levels of cortisol and adrenocorticotrophic hormone. However, he exhibited hypoglycemic coma 4 months later. Detailed endocrinological examinations using dynamic function tests indicated IAD. After commencement of corticosteroid replacement therapy, his symptoms resolved without complications.
Conclusions: To our knowledge, this is the first report of a hemodialysis patient with both IAD and primary hypothyroidism. This case highlights the importance of regular assessments of thyroid function for primary hypothyroidism in hemodialysis patients, even when they are asymptomatic. Furthermore, timely dynamic endocrine testing of hypothalamic-pituitary-adrenal function is needed to diagnose possible IAD in hemodialysis patients with symptoms suggestive of adrenal insufficiency, even in the absence of abnormal laboratory findings such as electrolyte imbalances or low morning blood levels of cortisol or adrenocorticotrophic hormone.

MeSH Keywords: Adrenal Insufficiency • Adrenocorticotrophic Hormone • Glomerulonephritis, IGA • Hemodialysis Units, Hospital • Hydrocortisone • Thyroxine

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/922376>

2261 3 1 24

Background

Primary hypothyroidism is a common disorder characterized by thyroid hormone deficiency due to abnormalities in the thyroid gland [1]. Although some patients are asymptomatic, the clinical manifestations of primary hypothyroidism include fatigue, lethargy, and cold intolerance. The prevalence of primary hypothyroidism is higher in patients with chronic kidney disease than in the general population, and a reduced glomerular filtration rate is associated with a higher prevalence of hypothyroidism [2]. Patients with end-stage renal disease (ESRD) who are undergoing long-term maintenance hemodialysis therapy also often exhibit primary hypothyroidism [3,4].

Isolated adrenocorticotrophic hormone deficiency (IAD) is a rare pituitary disorder characterized by central adrenal insufficiency with low or absent cortisol production, normal secretion of pituitary hormones other than adrenocorticotrophic hormone (ACTH) and, typically, an absence of structural pituitary defects [5]. The clinical manifestations of IAD include symptoms of adrenal insufficiency, such as anorexia, fatigue, and lethargy. Blood biochemistry analyses may also indicate mild hypoglycemia, anemia, lymphocytosis, eosinophilia, and electrolyte imbalances such as hyponatremia and normal-to-high potassium levels. IAD often causes acute life-threatening conditions such as adrenal crisis or hypoglycemic coma; thus, early diagnosis is important for prolonging survival. Additionally, only a few cases of IAD have been reported among hemodialysis patients [6–8].

Here, we report an unusual case in which a patient with ESRD who was undergoing long-term hemodialysis exhibited both IAD and primary hypothyroidism. In addition, we review previously reported cases of hemodialysis patients with IAD.

Case Report

An 84-year-old Japanese male who had been undergoing hemodialysis for 20 years was admitted to our hospital in March 2018 for hypoglycemic coma following a 4-month duration of anorexia, fatigue, and lethargy. The patient had a paternal family history of cerebral infarction. The patient did not drink alcohol or consume iodine-containing foods in excess. The patient's medical history was unremarkable until 52 years of age, when an annual health checkup revealed protein and blood in his urine; he was diagnosed with biopsy-proven immunoglobulin A (IgA) nephropathy. Although the patient received conservative medical treatment, his kidney function gradually deteriorated, and he started maintenance hemodialysis (thrice weekly) for ESRD at 62 years of age.

Subsequently, when the patient was in his 70s, a routine blood test detected slightly high serum thyroid-stimulating

hormone (TSH) levels with normal serum thyroid hormone levels. His serum TSH levels gradually increased, and a blood test performed in June 2016 (at 82 years of age) revealed high TSH (15.19 μ U/mL), low free thyroxine (FT₄; 0.68 ng/dL), and low free triiodothyronine (FT₃; 1.64 pg/mL) levels, indicating progression to primary hypothyroidism. However, the patient did not exhibit symptoms of hypothyroidism, such as fatigue, lethargy, or cold intolerance. The patient's medications included cilostazol, nalfurafine hydrochloride, calcium-containing phosphate binder, ferric citrate hydrate, and erythropoietin. Although he underwent dietary iodine restriction to improve his asymptomatic primary hypothyroidism [9], the disorder persisted. Thus, the patient started oral levothyroxine (75 μ g/day) in December 2016, and the dose was adjusted to maintain normal levels of serum thyroid hormones and TSH.

In November 2017, the patient developed anorexia, fatigue, and lethargy without a prodrome, such as head trauma or headache. Detailed examinations were performed the same month. Computed tomography of the abdomen showed no abnormalities in the liver, spleen, pancreas, or adrenal glands, except for atrophic kidneys; echocardiography showed normal cardiac function without left ventricular wall thickening or granular sparkling. Gastrofiberscopy revealed no abnormalities in the patient's esophagus, stomach, or small intestine; colonoscopy also detected no abnormalities; and immunohistochemical analysis using Congo Red staining detected no amyloid depositions in biopsy specimens of the gastric or colon mucosa. Blood tests revealed normal levels of electrolytes including sodium, potassium, and calcium, fasting plasma glucose (78 mg/dL), and morning basal cortisol (10.8 μ g/dL), as well as a slightly increased ACTH (73.5 pg/mL) level (electrochemiluminescence immunoassay) [10].

In March 2018, the patient was brought by ambulance to our hospital because of coma. In the emergency room, his body temperature, blood pressure, and pulse rate were 35.6°C, 146/78 mm Hg, and 67 beats/minute, respectively. A blood test revealed a low plasma glucose level (19 mg/dL). The patient rapidly recovered consciousness after an intravenous infusion of glucose and was admitted to our hospital for further examination and management.

On physical examination at admission, the patient had clear consciousness, and his height and body weight were 154 cm and 40.2 kg (body mass index, 17.0 kg/m²), respectively. No exophthalmos, megaloglossia, thyromegaly, chest rales, heart murmurs, finger tremors, skin rashes, or peripheral edema were detected. Blood tests performed the next morning (Table 1) showed that, although his serum cortisol level (9.4 μ g/dL) was within the normal reference range, it appeared relatively low based on a mild low fasting plasma glucose level (66 mg/dL); therefore, it was not possible to exclude the

Table 1. Blood chemistry at admission (March 2018).

Hematology					
Red blood cells	334×10 ⁴ /μL	(435–555)	Phosphorus	3.1 mg/dL	(2.7–4.6)
Hemoglobin	10.2 g/dL	(13.7–16.8)	Iron	77 μg/dL	(40–188)
Hematocrit	31.7%	(40.7–50.1)	Ferritin	155 ng/mL	(31–325)
White blood cells	5,000/μL	(3,300–8,600)	C-reactive protein	4.42 mg/dL	(0–0.14)
Neutrophils	44.8%		Intact parathyroid hormone	134 pg/mL	(10–65)
Lymphocytes	39.9%		Fasting plasma glucose	66 mg/dL	(70–109)
Eosinophils	9.1%		Immunoreactive insulin	<0.3 μU/mL	
Basophils	0.8%		Glycated hemoglobin	4.5%	(4.6–6.2)
Monocytes	5.4%		Thyroid-stimulating hormone	5.75 μIU/mL	(0.50–5.00)
Platelets	15.1×10 ⁴ /μL	(15.8–34.8)	Free triiodothyronine	1.51 pg/mL	(2.30–4.00)
Blood biochemistry			Free thyroxine	1.34 ng/dL	(0.90–1.70)
Total protein	5.9 g/dL	(6.6–8.1)	Thyroglobulin	58.4 ng/mL	(0–32.7)
Albumin	2.5 g/dL	(4.1–5.1)	Adrenocorticotrophic hormone	79.6 pg/mL	(7.2–63.3)
Urea nitrogen	26.6 mg/dL	(8.0–18.4)	Cortisol	9.4 μg/dL	(4.5–21.1)
Creatinine	5.52 mg/dL	(0.65–1.07)	Dehydroepiandrosterone sulfate	1,024 ng/mL	(50–2,530)
Sodium	142 mEq/L	(135–145)	Plasma renin activity	0.4 ng/mL/h	(0.2–2.3)
Potassium	4.2 mEq/L	(3.5–4.8)	Aldosterone	7.0 ng/dL	(3.0–15.9)
Chloride	108 mEq/L	(98–108)			
Calcium	8.4 mg/dL	(8.8–10.1)			

Blood samples were taken in the morning (9 AM) in a fasting state with the patient in a supine position (24 hours after receipt of maintenance hemodialysis). The patient was receiving thyroid hormone replacement therapy with oral levothyroxine (100 μg/day) for primary hypothyroidism. The reference range for each parameter is shown in parentheses.

possibility of adrenal insufficiency. The serum aldosterone level (7.0 ng/dL) was normal. The plasma ACTH level was slightly high (79.6 pg/mL). The patient had normal serum FT₄ (1.32 ng/dL) and slightly high TSH (5.75 μIU/mL) levels after taking oral levothyroxine (100 μg/day). His blood electrolyte levels, including sodium, potassium, and calcium, were normal.

A rapid ACTH stimulation test showed a low cortisol response; however, adequate cortisol release was observed during a prolonged ACTH stimulation test (Table 2A, 2B), suggesting central adrenal insufficiency. Dynamic tests assessing the secretion of anterior pituitary hormones showed normal responses of growth hormone, TSH, and prolactin, as well as age-appropriate secretion of luteinizing hormone and follicle-stimulating hormone; although the basal ACTH level was high, no sufficient ACTH or cortisol release was observed after a corticotropin-releasing hormone load (Table 2C). These findings were suggestive of IAD accompanied by immunoreactive but biologically inactive ACTH [11,12].

Brain magnetic resonance imaging (MRI) revealed no abnormalities in the hypothalamus, hypophyseal stalk, or pituitary gland (Figure 1). Ultrasonography of the neck revealed no abnormalities in the size or echogenicity of the thyroid gland, without a tumor. Fine-needle aspiration cytology of both lobes of the thyroid gland was performed to investigate the etiology of the primary hypothyroidism, which revealed normal thyroid follicular cells with no nuclear atypia; no abnormal findings suggestive of thyroiditis or amyloid depositions were detected.

The patient tested negative for pituitary autoantibody, thyroglobulin autoantibody, thyroid peroxidase autoantibody, TSH-binding inhibitory immunoglobulin, glutamic acid decarboxylase autoantibody, adrenocortical autoantibody, and anti-nuclear autoantibody. Human leukocyte antigen typing showed the presence of A*02/26, B*15/40, and C*01: 02/08: 01 class I genes and DRB1*09: 01/15: 01, DQB1*03: 03/06: 02, DQA1*01: 02/03: 02, and DPB1*02: 01/05: 01 class II genes.

Table 2A. Endocrinological investigation: Rapid adrenocorticotrophic hormone stimulation test (March 2018).

	Time (minutes)		
	0	30	60
Cortisol (µg/dL)	7.6	8.9	9.3

Synthetic adrenocorticotrophic hormone 1–24 (0.25 mg tetracosactide acetate) was administered intravenously in the morning (9 AM).

Table 2B. Endocrinological investigation: Prolonged adrenocorticotrophic hormone stimulation test (March 2018).

	Reference range	Before	After
Cortisol (µg/dL)	4.5–21.1	9.1	24.2
Adrenocorticotrophic hormone (pg/mL)	7.2–63.3	98.1	34.2

Blood samples were collected each morning (9 AM) on the days before and after intramuscular administration of synthetic adrenocorticotrophic hormone 1–24 (1.0 mg/day tetracosactide zinc) for 3 days.

Table 2C. CRH/GRF/TRH/LHRH stimulation test (March 2018).

	Time (minutes)					
	0	15	30	60	90	120
Adrenocorticotrophic hormone (pg/mL)	94.7	106.0	120.0	107.0	93.6	100.0
Cortisol (µg/dL)	12.0	11.2	11.8	12.9	13.4	13.9
Growth hormone (ng/mL)	1.9	5.3	7.0	9.8	11.3	7.4
Thyroid-stimulating hormone (µIU/mL)	4.17	16.04	19.36	19.93	17.66	16.09
Prolactin (ng/mL)	10.4	39.6	44.9	44.2	44.0	43.1
Luteinizing hormone (mIU/mL)	10.8	19.8	24.2	33.4	36.3	38.3
Follicle-stimulating hormone (mIU/mL)	22.2	24.2	26.4	29.8	31.8	34.9

The following synthetic hypothalamic hormones were administered intravenously in the morning (9 AM): human corticotropin-releasing hormone (CRH; 100 µg), growth hormone-releasing factor (GRF; 100 µg), thyrotropin-releasing hormone (TRH; 500 µg), and luteinizing hormone-releasing hormone (LHRH; 100 µg).

The patient began corticosteroid replacement therapy with oral hydrocortisone (15 mg/day) on day 10 of admission. His anorexia, fatigue, lethargy, and fasting hypoglycemia resolved completely. He was discharged 42 days after admission.

A growth hormone-releasing peptide-2 loading test [13] performed in March 2019 showed normal growth hormone release; ACTH release was apparently normal, whereas no adequate cortisol response was observed (Table 2D). The patient's plasma renin activity (0.5 ng/mL/hour) and serum aldosterone level (9.2 ng/dL) were normal, but his serum dehydroepiandrosterone sulfate level (393 ng/dL) [14] was decreased compared with 1 year earlier (1024 ng/dL; Table 1). These findings confirmed the diagnosis of IAD.

The patient's subsequent clinical course during maintenance hemodialysis and hormone replacement therapy with oral hydrocortisone and levothyroxine has been uneventful.

Discussion

Table 3 summarizes the characteristics of patients with ESRD who were undergoing maintenance hemodialysis and exhibited IAD. The cases include both male and female adults with different primary kidney diseases who were diagnosed with IAD after 3–22 years of regular hemodialysis. They presented with adrenal insufficiency symptoms, including anorexia and fatigue with or without subsequent hypoglycemic coma; the time from the appearance of adrenal insufficiency symptoms to IAD diagnosis varied from 4 months to more than 1 year. To the best of our knowledge, this is the first report of a hemodialysis patient with both IAD and primary hypothyroidism.

Diagnosing IAD in patients with ESRD who are undergoing hemodialysis can be challenging. Firstly, hemodialysis patients usually experience renal anemia and often show eosinophilia [15,16], which are also symptoms of IAD [5]. Secondly,

Figure 1. Magnetic resonance imaging of the pituitary gland. Plain T1-weighted images (A) coronal plane and (B) sagittal plane revealed no abnormalities in the hypothalamus, hypophyseal stalk, or pituitary gland (arrows).

Table 2D. GHRP-2 stimulation test (March 2019).

	Time (minutes)				
	0	15	30	45	60
Adrenocorticotrophic hormone (pg/mL)	35.5	51.2	48.7	47.1	43.5
Cortisol (µg/dL)	2.6	3.0	3.1	2.9	2.9
Growth hormone (ng/mL)	0.3	27.3	39.5	33.6	26.2

Growth hormone-releasing peptide-2 (GHRP-2; 100 µg) was administered intravenously in the morning (9 AM). The test was conducted after brief cessation of corticosteroid replacement therapy with oral hydrocortisone (15 mg/day).

conventional hemodialysis therapy maintains adequate circulating volume and blood electrolyte levels, thereby masking an otherwise obvious electrolyte imbalance attributable to IAD, such as hyponatremia or normal-to-high potassium levels. In addition to these factors, our patient had a normal morning blood cortisol level and a high ACTH level at the time of diagnosis with IAD, which could also be explained by a combination of incomplete corticotroph failure and immunoreactive but biologically inactive ACTH [11,12], which delayed the diagnosis of IAD. Thus, this case highlights the importance of timely dynamic endocrine testing of hypothalamic-pituitary-adrenal function to provide early diagnosis of possible IAD in hemodialysis patients with symptoms suggestive of adrenal insufficiency, such as anorexia, fatigue, and lethargy, even when they do not exhibit electrolyte imbalances or low morning blood cortisol or ACTH levels.

Patients with ESRD on long-term hemodialysis tend to exhibit primary hypothyroidism and other endocrinopathies, such

as growth retardation and hypogonadism [17,18]; however, few studies have shown any susceptibility to ACTH deficiency in hemodialysis patients. In general, IAD can occur in association with traumatic injury, radiation therapy for a brain tumor, hypophysitis, or pituitary autoimmunity. Pituitary autoimmunity is also often accompanied by other organ-specific autoimmune disorders as a component of autoimmune polyglandular syndromes (APS) [5]. In the present case, the patient did not experience head trauma, a brain tumor, or radiation therapy, and exhibited no morphological pituitary defect. Additionally, he did not have endocrine autoimmune diseases, such as autoimmune thyroid diseases or type 1 diabetes mellitus. However, he had a history of IgA nephropathy. Autoimmunity in the kidney is suggested to play an important role in the pathogenesis of IgA nephropathy [19,20]. Thus, pituitary autoimmunity associated with APS is a possible explanation for the IAD in our case.

Table 3. Summary of published data from patients with ESRD who were on maintenance hemodialysis and exhibited IAD.

Ref.	Sex	Age at starting dialysis (years)	ESRD			IAD										Other findings
			Cause	HD frequency (/wk)	Age at diagnosis (years)	Symptoms	Time from first clinical symptoms to diagnosis (months)	Basal blood ACTH (pg/mL)	Basal blood cortisol (µg/dL)	Blood sodium (mEq/L)	Blood potassium (mEq/L)	MRI findings of the pituitary gland	Pituitary autoantibodies	Thyroid autoantibodies		
[6]	F	24	Chronic glomerulonephritis	Thrice	44	Anorexia, fatigue, fever, and hypotension	N.D.	<5.0	6.5	N.D.	N.D.	No abnormality	Negative	Negative	Hypercalcemia, esophageal ulcer, chronic pancreatitis	
[7]	M	59	Diabetic nephropathy	Thrice	62	Hypoglycemic coma following anorexia and fatigue	15	4.3	<2.0	137	3.7	No abnormality	Negative	N.D.	Alcoholic liver cirrhosis and chronic pancreatitis, type 2 diabetes mellitus	
[8]	M	51	Chronic glomerulonephritis	Thrice	58	Anorexia and fatigue	N.D. in detail (a long duration)	2.9	<1.0	N.D.	N.D.	N.D.	N.D.	N.D.	Hypercalcemia	
Present case	M	62	IgA nephropathy	Thrice	84	Hypoglycemic coma following anorexia, fatigue, and lethargy	4	79.6	9.4	142	4.2	No abnormality	Negative	Negative	Primary hypothyroidism	

ACTH – adrenocorticotrophic hormone; ESRD – end-stage renal disease; F – female; HD – hemodialysis; IAD – isolated adrenocorticotrophic hormone deficiency; IgA – immunoglobulin A; M – male; MRI – magnetic resonance imaging; N.D. – not described; wk – week.

Although secondary adrenal insufficiency is caused by a deficiency of ACTH secretion from disturbed corticotrophs, patients may present with high plasma ACTH levels attributable to the secretion of ACTH molecules that lack steroidogenic bioactivity, but conserve immunoreactivity. For example, there have been 2 reported cases of secondary adrenal insufficiency in children with high plasma ACTH levels, due to the expression of immunoreactive but biologically inactive ACTH caused by mutations in the pro-opiomelanocortin gene [11]. An elderly patient with Hashimoto thyroiditis and IAD exhibiting high plasma ACTH levels has also been described, in whom pituitary autoimmunity was likely responsible for disturbed corticotrophs secreting immunoreactive but biologically inactive ACTH [12]. However, all previous reports of hemodialysis patients with IAD were characterized by low plasma ACTH levels, with the exception of our patient (Table 3). Thus, the expression of immunoreactive but biologically inactive ACTH in our patient, as indicated by endocrinological laboratory test results (Table 2), may have been related to factors other than ESRD or hemodialysis, such as pituitary autoimmunity.

Primary hypothyroidism is commonly caused by chronic autoimmune thyroiditis; less frequent causes include neck irradiation or surgery, excessive iodine intake, and certain drugs, such as interferons, amiodarone, and lithium [1]. In addition, many factors associated with ESRD/hemodialysis-related primary hypothyroidism have been suggested, such as endothelial damage, oxidative stress, retention of excessive iodine, and/or iron overload [9,21–23]. Importantly, hypothyroidism is associated with higher mortality in hemodialysis patients, which may be ameliorated by thyroid hormone replacement therapy [4]. The present patient did not exhibit any of the known causal factors for primary hypothyroidism; however, he developed gradual-onset primary hypothyroidism without obvious symptoms after more than 10 years of hemodialysis. Thus, this case of ESRD/hemodialysis-related primary hypothyroidism highlights the importance of regular assessments of thyroid function for the detection of primary hypothyroidism in patients undergoing hemodialysis, even when they are asymptomatic.

ESRD patients undergoing hemodialysis for more than 10 years may have dialysis-related (β 2-microglobulin) amyloidosis that primarily affects the osteoarticular tissues and occasionally involves systemic organs such as the tongue, heart, and intestinal tracts [24]. However, there are few reports of dialysis-related amyloidosis in the endocrine organs or associated endocrinopathies. In the present case, a series of physical, radiological, and pathological examinations did not detect abnormal findings indicative of amyloid depositions in any of the systemic or endocrine organs, including the pituitary and thyroid glands.

Conclusions

We describe a patient with ESRD who was undergoing long-term hemodialysis and exhibited asymptomatic primary hypothyroidism; this was followed by IAD, which manifested as hypoglycemic coma following a 4-month duration of anorexia, fatigue, and lethargy. No direct causal link was found between IAD and ESRD/hemodialysis-related primary hypothyroidism; however, polyglandular autoimmunity may have been involved in the development of both IAD and IgA nephropathy, whereas the IgA nephropathy led to ESRD. This case highlights the importance of regular assessments of thyroid function for the detection of primary hypothyroidism in hemodialysis patients, even when they are asymptomatic. Furthermore, timely dynamic endocrine testing of hypothalamic-pituitary-adrenal function is necessary for early diagnosis of IAD in hemodialysis patients with symptoms suggestive of adrenal insufficiency, even those who do not exhibit abnormal laboratory findings such as electrolyte imbalances or low morning blood levels of cortisol or ACTH.

References:

- Chaker L, Bianco AC, Jonklaas J, Peeters RP: Hypothyroidism. *Lancet*, 2017; 390: 1550–62
- Lo JC, Chertow GM, Go AS, Hsu CY: Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease. *Kidney Int*, 2005; 67: 1047–52
- Paudel K: Prevalence and clinical characteristics of hypothyroidism in a population undergoing maintenance hemodialysis. *J Clin Diagn Res*, 2014; 8: MC01–4
- Rhee CM, Alexander EK, Bhan I, Brunelli SM: Hypothyroidism and mortality among dialysis patients. *Clin J Am Soc Nephrol*, 2013; 8: 593–601
- Andrioli M, Pecori Giraldi F, Cavagnini F: Isolated corticotrophin deficiency. *Pituitary*, 2006; 9: 289–95
- Kato A, Shinozaki S, Goga T, Hishida A: Isolated adrenocorticotrophic hormone deficiency presenting with hypercalcemia in a patient on long-term hemodialysis. *Am J Kidney Dis*, 2003; 42: E32–36
- Tanaka M, Suganuma K, Funase Y et al: Hypoglycaemic coma due to adrenal failure in a chronic haemodialysis patient. *NDT Plus*, 2011; 4: 36–38
- Sakao Y, Sugira T, Tsuji T et al: Clinical manifestation of hypercalcemia caused by adrenal insufficiency in hemodialysis patients: A case-series study. *Intern Med*, 2014; 53: 1485–90
- Sanai T, Inoue T, Okamura K et al: Reversible primary hypothyroidism in Japanese patients undergoing maintenance hemodialysis. *Clin Nephrol*, 2008; 69: 107–13
- Abe M, Araki S, Tawaragi M et al: [Fundamental evaluation of ACTH measurement using automated electrochemiluminescence-immunoassay system, ECLusys® 2010.] *Igaku To Yakugaku*, 2007; 57: 239–244 [in Japanese]
- Samuels ME, Gallo-Payet N, Pinard S et al., FORGE Canada Consortium: Bioinactive ACTH causing glucocorticoid deficiency. *J Clin Endocrinol Metab*, 2013; 98: 736–42
- Ohara N, Kaneko M, Kuriyama H et al: Isolated adrenocorticotropin deficiency concomitant with Graves' disease: A case report and literature review. *Intern Med*, 2016; 55: 2649–58
- Arimura H, Hashiguchi H, Yamamoto K et al: Investigation of the clinical significance of the growth hormone-releasing peptide-2 test for the diagnosis of secondary adrenal failure. *Endocr J*, 2016; 63: 533–44
- Sayed Kassem L, El Sibai K, Chaiban J et al: Measurements of serum DHEA and DHEA sulphate levels improve the accuracy of the low-dose cosyntropin test in the diagnosis of central adrenal insufficiency. *J Clin Endocrinol Metab*, 2012; 97: 3655–62
- Chen TK, Knicely DH, Grams ME: Chronic kidney disease diagnosis and management: A review. *JAMA*, 2019; 322: 1294–304

Acknowledgments

The authors thank the clinical laboratory technicians of Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, for their technical support.

Department and Institution where work was done

Department of Endocrinology and Metabolism, Uonuma Institute of Community Medicine, Niigata University Medical and Dental Hospital, Minamiuonuma, Niigata, Japan

Conflicts of interest

None.

Abbreviations

ACTH – adrenocorticotrophic hormone; **AI** – adrenal insufficiency; **CRH** – corticotropin-releasing hormone; **ESRD** – end-stage renal disease; **FT₃** – free triiodothyronine; **FT₄** – free thyroxine; **GHRP-2** – growth hormone releasing-peptide-2; **GRF** – growth hormone-releasing factor; **HD** – hemodialysis; **IAD** – isolated adrenocorticotrophic hormone deficiency; **IgA** – immunoglobulin A; **LHRH** – luteinizing hormone-releasing hormone; **MRI** – magnetic resonance imaging; **N.D.** – not described; **PH** – primary hypothyroidism; **TRH** – thyrotropin-releasing hormone; **TSH** – thyroid-stimulating hormone; **wk** – week.

16. Hildebrand S, Corbett R, Duncan N, Ashby D: Increased prevalence of eosinophilia in a hemodialysis population: Longitudinal and case control studies. *Hemodial Int*, 2016; 20: 414–20
17. Bonomini V, Orsoni G, Sorrentino MA, Todeschini P: Hormonal changes in hemodialysis. *Blood Purif*, 1990; 8: 54–68
18. Gungor O, Kocyigit I, Carrero JJ, Yilmaz MI: Hormonal changes in hemodialysis patients: Novel risk factors for mortality? *Semin Dial*, 2017; 30: 446–52
19. Novak J, Renfrow MB, Gharavi AG, Julian BA: Pathogenesis of immunoglobulin A nephropathy. *Curr Opin Nephrol Hypertens*, 2013; 22: 287–94
20. Lai KN, Tang SC, Schena FP et al: IgA nephropathy. *Nat Rev Dis Primers*, 2016; 2: 16001
21. Malyszko J, Malyszko JS, Pawlak K, Mysliwiec M: Thyroid function, endothelium, and inflammation in hemodialyzed patients: Possible relations? *J Ren Nutr*, 2007; 17: 30–37
22. Velayeti J, Mansourian AR, Mojerloo M, Marjani A: Evaluation of oxidative stress and thyroid hormone status in hemodialysis patients in Gorgan. *Indian J Endocrinol Metab*, 2016; 20: 348–53
23. el-Reshaid K, Seshadri MS, Hourani H et al: Endocrine abnormalities in hemodialysis patients with iron overload: Reversal with iron depletion. *Nutrition*, 1995; 11(5 Suppl.): 521–26
24. Saito A, Gejyo F: Current clinical aspects of dialysis-related amyloidosis in chronic dialysis patients. *Ther Apher Dial*, 2006; 10: 316–20