Carbamazepine-Induced Drug-Induced Hypersensitivity Syndrome With Primary Adrenal Insufficiency: A Case Report

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Drug-induced hypersensitivity syndrome (DIHS), also known as drug reaction with eosinophilia and systemic symptoms, is a severe adverse reaction involving multiple organs. We describe a case of carbamazepine (CBZ)-induced DIHS with rare primary endocrine complications. A 71-year-old Japanese man developed generalized erythroderma with systemic symptoms 6 weeks after the initiation of CBZ at 200 mg/day for trigeminal neuralgia. Clinical evaluation revealed *HLA-A31:01 positivity, marked eosinophilia, elevated inflammatory markers, and multiorgan involvement, including acute interstitial nephritis and primary hypothyroidism. Primary adrenal insufficiency became clinically evident after levothyroxine administration. Chest computed tomography revealed enlarged cervical and axillary lymph nodes, an abscess in the right upper lobe, and emphysema in both lungs. Although HHV-6 reactivation was not detected, the patient's clinical course was consistent with that of atypical DIHS. The patient was treated by immediate discontinuation of CBZ and initiation of systemic corticosteroids after thyroid hormone replacement therapy, which resulted in clinical improvement. To our knowledge, this is the first report of primary adrenal insufficiency as a manifestation of CBZ-induced DIHS in Japan. Carriers of *HLA-A**31:01 require comprehensive endocrine and systemic monitoring because DIHS can precipitate rare primary endocrine gland failure. Pre-prescription HLA genotyping remains an essential preventive strategy for this high-risk population.**

Key words: carbamazepine, drug-induced hypersensitivity syndrome, drug reaction with eosinophilia and systemic symptoms, *HLA-A31:01, adrenal insufficiency**

INTRODUCTION

Drug-induced hypersensitivity syndrome (DIHS), also known as drug reaction with eosinophilia and systemic symptoms (DRESS), is a T cell-mediated severe cutaneous adverse reaction with a clinical latency of 2 to 6 weeks [1]. This multisystem inflammatory disorder is characterized by the classic triad of fever, cutaneous eruption, and involvement of internal organs, including the liver, kidneys, heart, and lungs [1]. Carbamazepine (CBZ), an aromatic anticonvulsant commonly prescribed for seizure control and chronic pain, is among the five most frequent causes of DIHS worldwide [1, 2].

Recent advances in pharmacogenomics have established *HLA-A**31:01 as a major susceptibility allele for severe CBZ-induced adverse reactions in Northern European and East Asian populations [3]. The frequency of *HLA-A**31:01 in Japanese individuals is approximately 9%, and carriers have a 10.8-fold increased risk of severe cutaneous adverse events [4]. The proposed pathogenic mechanism involves the direct binding of CBZ metabolites to the HLA molecule, resulting in activation of drug-specific cytotoxic T lymphocytes (CTLs) and subsequent multi-organ damage [5].

The predominant features of DIHS include hepatomegaly (75%), fever (90%), and facial edema (76%), with less frequent involvement of the kidneys (37%) and lungs (32%) [6]. Endocrine complications in DIHS are exceptionally rare; hypothyroidism occurs in only 1.7% of reported cases, whereas primary adrenal insufficiency has not been previously documented in the Japanese literature in association with CBZ-induced DIHS. We report a unique case of CBZ-induced DIHS complicated by acute interstitial nephritis (AIN), primary hypothyroidism, and primary adrenal insufficiency that developed after initiation of thyroid hormone replacement therapy.

CASE REPORT

Patient Presentation and Clinical Course

A 71-year-old Japanese man was admitted to our hospital with dyspnea and generalized skin eruptions. The patient had been prescribed CBZ at a dose of 200 mg/day approximately 6 weeks prior to admission for the management of intractable trigeminal neuralgia. One week prior to admission, he developed a widespread skin rash involving the entire body, followed by progressive malaise, anorexia, and dyspnea. The patient's medical history was unremarkable, with no prior drug allergies or significant comorbidities. His personal history was notable only for smoking cessation 20 years earlier and occasional alcohol consumption.

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Physical examination upon admission revealed that the patient was alert (Japan Coma Scale I−10) but hemodynamically compromised, with a blood pressure of 80/43 mmHg, a body temperature of 35.6°C, and oxygen saturation of 99% on 10 L/min supplemental oxygen. Characteristic skin findings included generalized erythroderma with thick white scales, predominantly affecting the face and trunk. Cervical and axillary lymphadenopathy was observed. Pulmonary auscultation revealed no crackles, and the abdominal examination was unremarkable.

Laboratory Investigations

Initial laboratory tests revealed significant abnormalities. Complete blood count demonstrated marked leukocytosis (white blood cell count of 20,600/μL) with a prominent left shift and an initial reported eosinophil count of 0%. Notably, atypical lymphocytes were prominent on differential examination. Biochemical analysis indicated evidence of multiorgan involvement, as reflected by the following results: elevated transaminase levels, with aspartate aminotransferase at 72 U/L and alanine aminotransferase at 62 U/L; an elevated alkaline phosphatase level of 276 U/L; indicators of acute kidney injury, including a serum creatinine level of 1.51 mg/dL and blood urea nitrogen level of 53 mg/dL; and increased lactate dehydrogenase at 493 U/L. Coagulation studies showed mild prolongation of prothrombin time, with a PT of 18.8 s and an international normalized ratio of 1.56, as well as an elevated D-dimer level of 31.7 μg/mL.

Endocrine evaluation indicated primary hypothyroidism. Serial thyroid function tests showed a thyroid-stimulating hormone (TSH) level of 19.74 μIU/mL and free T4 (FT4) of 0.69 ng/dL (FT3 1.32 pg/mL) on day 10. TSH levels continued to rise, reaching a peak of 59.96 μIU/mL (FT4 0.70 ng/dL, FT3 1.80 pg/mL) on day 28 during repeat testing.

The baseline cortisol level was 16.5 μg/dL (reference threshold > 8 μg/dL), and the adrenocorticotropic hormone (ACTH) level was 50.1 pg/mL, which excluded adrenal insufficiency at admission. Inflammatory markers were significantly elevated, as demonstrated by a C-reactive protein level of 16.96 mg/dL. Serial electrolyte measurements revealed the following sodium and potassium values: day 1, Na 155 mEq/L and K 4.4 mEq/L (hypertonic dehydration); day 14, Na 136 mEq/L and K 4.1 mEq/L; day 25, Na 131 mEq/L and K 4.1 mEq/L (hyponatremia with clinical adrenal insufficiency); day 35, Na 136 mEq/L and K 4.3 mEq/L (normalization after hydrocortisone initiation). On day 28, assessment of the mineralocorticoid axis revealed a plasma aldosterone concentration (PAC) of < 10 pg/mL, confirming aldosterone deficiency. Plasma renin activity (PRA) was 0.3 ng/mL/hr (reference 0.7−3.3 ng/mL/hr). This low-normal PRA was likely attributable to the suppressive effects of dexamethasone initiated two days prior to and concurrent with fluid resuscitation, rather than true renin suppression. The low PAC level, together with progressive hyponatremia, supports mineralocorticoid deficiency as a component of primary adrenal insufficiency in this case. Following transition to hydrocortisone 20 mg/day, serum sodium normalized without fludrocortisone supplementation, consistent with the intrinsic mineralocorticoid activity of hydrocortisone at physiologic replacement doses.

Imaging Findings

Chest computed tomography revealed enlarged cervical and axillary lymph nodes, a lung abscess in the right upper lobe, and emphysema in both lungs. Abdominal imaging excluded hepatosplenomegaly, cholecystitis, and other acute abdominal pathologies.

Genetic and Viral Testing

Sequence-based HLA genotyping confirmed the presence of the *HLA-A**31:01 allele. The drug lymphocyte stimulation test was positive for CBZ, confirming drug-specific T-cell activation. Notably, polymerase chain reaction testing for human herpesvirus 6 (HHV-6) DNA in peripheral blood was negative, which is atypical for DIHS but may reflect the timing of viral reactivation, viral clearance, or genuinely low viral loads at the time of testing.

Treatment and Hospital Course

Upon admission, CBZ was immediately discontinued, and empiric antimicrobial therapy was initiated with vancomycin, piperacillin/tazobactam, and metronidazole for the lung abscess and possible sepsis. Thyroid hormone replacement was initiated with levothyroxine at an initial dose of 25 μg per day and titrated up to 100 μg per day.

The baseline morning cortisol level on day 1, measured prior to any corticosteroid administration, was 16.5 μg/dL, and the ACTH level was 50.1 pg/mL, indicating preserved adrenal reserve at admission. Dexamethasone 0.5 mg once daily was initiated on day 26 in response to clinical deterioration. A repeat cortisol measurement on day 27, following only a single dose of dexamethasone, revealed a critically low value of 3.94 μg/dL with ACTH 53.6 pg/mL. Four-hormone dynamic stimulation testing on day 28 confirmed primary adrenal insufficiency, as demonstrated by a blunted cortisol response (baseline 3.94 μg/dL, 30-min 4.01 μg/dL, 60-min 3.89 μg/dL). The minimal dexamethasone exposure (one dose, 0.5 mg) was insufficient to suppress the hypothalamic-pituitary-adrenal (HPA) axis, confirming that the critically low cortisol level reflected true primary adrenal failure rather than iatrogenic suppression.

Approximately 2 weeks after levothyroxine initiation, the patient exhibited clinical features of acute adrenal insufficiency, including persistent hypotension unresponsive to volume resuscitation and increasing fatigue (Fig. 1). At this stage, repeat cortisol measurement was critically low at 3.94 μg/dL, with an ACTH level of 53.6 pg/mL. Within 48 h of initiating dexamethasone therapy, the patient's fever subsided, and the systemic skin eruption improved further. Four-hormone dynamic stimulation testing confirmed primary adrenal insufficiency, as evidenced by a blunted cortisol response to ACTH (ACTH stimulation test: baseline cortisol 3.94 μg/dL, 30-min 4.01 μg/dL, 60-min 3.89 μg/dL).

The adrenal hormone replacement was switched from dexamethasone to hydrocortisone. The temporal relation between levothyroxine administration and the manifestation of adrenal insufficiency symptoms is

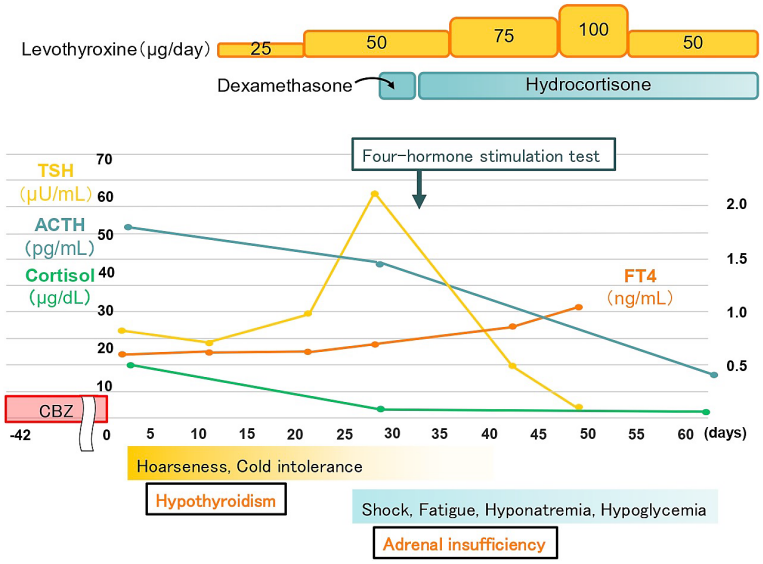

Fig. 1 Clinical course of the patient, including endocrine evaluation.
Note the temporal relation between levothyroxine initiation (day 12) and the clinical manifestation of adrenal insufficiency (day 26), demonstrating the unmasking of previously compensated adrenal insufficiency by accelerated thyroid hormone-induced metabolism.

noteworthy, as thyroid hormone replacement unmasks and exacerbates adrenal insufficiency by accelerating tissue metabolism, particularly when adrenal reserve is critically compromised. This clinical sequence underscores the need to assess adrenal function before or concurrently with thyroid hormone supplementation in patients with DIHS and endocrine involvement.

Over the subsequent hospital course, the patient demonstrated gradual clinical improvement, with progressive resolution of the rash, normalization of inflammatory markers, and stabilization of renal function. Eosinophil counts, which were initially suppressed (0%), subsequently rose to 45%–60% during the clinical course, consistent with the characteristic late phase of DIHS. The patient was ultimately discharged in stable condition on maintenance doses of levothyroxine 50 μg/day, hydrocortisone 20 mg/day (administered in divided doses), and dexamethasone 0.5 mg/day at night, with plans for outpatient endocrinology follow-up and gradual corticosteroid tapering.

Follow-up Assessment

At the 3-month follow-up, thyroid function tests indicated normalization with levothyroxine at 50 μg/day (TSH 1.20 μIU/mL, FT4 1.46 ng/dL, FT3 2.77 pg/mL). During hospitalization, levothyroxine was titrated to 100 μg/day, resulting in improved thyroid function by day 42 (TSH 3.71 μIU/mL, FT4 1.09 ng/dL, FT3 1.81 pg/mL). The dose was then reduced to a maintenance level of 50 μg/day.

At the 6-month follow-up, the patient continued hydrocortisone therapy at 15 mg/day, reduced from the initial 20 mg/day, and exhibited a plasma ACTH concentration of 4.5 pg/mL. This suppressed ACTH level indicates inhibition of the HPA axis by exogenous hydrocortisone and should not be considered evidence of adrenal recovery. A rapid ACTH stimulation test to formally evaluate adrenal functional recovery was not conducted at this visit, which constitutes a limitation of this report. Whether adrenal insufficiency in this case is due to permanent gland destruction or potentially reversible immune-mediated injury remains to be clarified by future testing. The patient's clinical status was stable, with effective blood pressure control and complete resolution of all cutaneous symptoms.

DISCUSSION

This case report presents multiple clinically significant features that enhance our understanding of CBZ-induced DIHS in the context of *HLA-A**31:01 positivity.

Pathogenic Mechanism and HLA Association

DIHS pathogenesis involves a complex interplay between drug-specific immune activation and viral factors. The prevailing model proposes that CBZ and its reactive metabolites undergo hapten processing and bind directly to HLA molecules in the context of *HLA-A**31:01 [3, 5]. The drug-HLA complex is then presented to CD8 + T cells via antigen-presenting cells, resulting in the generation and clonal expansion of CBZ-specific CTLs [5]. These activated CTLs subsequently infiltrate target tissues and mediate multiorgan inflammation by releasing proinflammatory cytokines, including interferon-γ, tumor necrosis factor-α, and interleukins.

The viral reactivation component of DIHS, typically involving HHV-6, is thought to occur 2–3 weeks into the clinical course and amplify the systemic inflammatory response by further activating CTLs and increasing cytokine production [1, 7]. The absence of HHV-6 DNA positivity in this case was unusual but not unprecedented. Negative HHV-6 findings may reflect (1) the timing of viral testing relative to the peak of viral replication, (2) spontaneous viral clearance prior to testing, (3) genuinely low viral loads that escape detection, or (4) atypical DIHS driven primarily by drug-specific immunity without significant viral participation [7].

Multi-Organ Manifestations

The clinical presentation of this patient demonstrated multi-organ involvement typical of severe DIHS. Erythroderma with facial edema and cervical lymphadenopathy represents cutaneous and lymphoid

manifestations.

AIN as a manifestation of CBZ-induced DIHS is well documented in the international literature and occurs in approximately 37% of DIHS cases [6]. The acute elevation in serum creatinine and blood urea nitrogen in this patient, coupled with the clinical and imaging exclusion of alternative etiologies and clear temporal relation to drug exposure, with resolution after cessation of CBZ and initiation of corticosteroid therapy, supports a diagnosis of AIN.

Rare Endocrine Involvement

The occurrence of both primary hypothyroidism and adrenal insufficiency in CBZ-induced DIHS is a particularly notable and unusual presentation. Primary adrenal insufficiency associated with CBZ-induced DIHS has not been previously reported in Japan.

Deng *et al*. systematically investigated endocrine sequelae in 45 DIHS patients and found that 8.8% developed autoimmune endocrine disorders. Three patients exhibited both fulminant type 1 diabetes mellitus (T1DM) and Hashimoto's thyroiditis (Autoimmune thyroid disease: AITD), meeting criteria for autoimmune polyendocrine syndrome type III (APS-III). A literature review identified seven additional cases involving more than two endocrine glands [9]. The current case, characterized by concurrent primary hypothyroidism and primary adrenal insufficiency, further broadens the spectrum of multi-endocrine involvement in DIHS beyond the frequently reported AITD-T1DM combination. Deng *et al*. proposed that regulatory T-cell (Treg) dysfunction following DIHS resolution, driven by Treg exhaustion from repeated viral reactivation, enables the activation of autoreactive T cells and provides a mechanistic explanation for organ-specific autoimmune endocrinopathies [9]. This shared Treg dysfunction may also account for the multi-endocrine phenotype observed in the current case.

The absence of anti-thyroid peroxidase and anti-thyroglobulin antibodies in this patient is consistent with nonautoimmune thyroid dysfunction and aligns with prior reports of DRESS-associated hypothyroidism in which direct CTL-mediated thyroid injury — analogous to hepatic, renal, and pulmonary DIHS involvement — occurs without detectable autoantibody production. Indeed, Tempark *et al*., reviewing 51 DRESS-associated thyroid dysfunction cases, noted that approximately 29% were classified as "possible/compatible with Hashimoto's thyroiditis" despite negative antibodies, and 5.9% as non-specific hypothyroidism, underscoring that seronegative thyroid injury is a recognized phenotype of DRESS [10]. The differential diagnosis also includes NTIS, a functional suppression of thyroid hormone production during critical illness; however, the markedly elevated TSH (peak 59.96 μIU/mL), persistently low FT4, and relatively preserved FT3 in this case are atypical for NTIS, which characteristically presents with low-to-normal TSH. The lack of spontaneous thyroid function recovery following clinical improvement and the persistent requirement for levothyroxine at three-month follow-up provide stronger evidence for true primary thyroid dysfunction rather than transient NTIS. Two limitations warrant acknowledgment: reverse T3 was not measured, precluding definitive biochemical exclusion of NTIS; and serial anti-thyroid antibody measurements were not repeated at follow-up visits, leaving open the possibility of delayed autoantibody seroconversion — a phenomenon documented months after DRESS resolution through Treg dysfunction-mediated liberation of autoreactive B cells [9].

The simultaneous occurrence of primary adrenal insufficiency is particularly remarkable, given its rarity. The pathogenic mechanism likely involves direct infiltration of the adrenal cortex by drug-specific CTLs, leading to destruction of ACTH-responsive steroidogenic cells. The extremely low baseline cortisol level (3.94 μg/dL) with elevated ACTH, despite low-dose exogenous corticosteroid therapy, supports a diagnosis of primary adrenal insufficiency. Concurrent mineralocorticoid deficiency, indicated by PAC less than 10 pg/mL and progressive hyponatremia (nadir sodium 131 mEq/L on day 25), further supports the presence of global adrenocortical dysfunction. The sustained normokalemia and resolution of hyponatremia with hydrocortisone alone, without fludrocortisone supplementation, demonstrate that hydrocortisone at physiologic replacement doses provides adequate mineralocorticoid activity.

Critically, acute adrenal insufficiency became clinically evident only after the initiation of levothyroxine therapy. This sequence reflects a well-recognized clinical principle: in patients with simultaneous thyroid and adrenal dysfunction, thyroid hormone replacement must be deferred or undertaken cautiously with concurrent adrenal steroid supplementation. Thyroid hormones accelerate tissue metabolism and increase cortisol clearance; when adrenal reserve is critically compromised, this metabolic acceleration unmasks and precipitates acute adrenal insufficiency symptoms, including refractory hypotension and shock. This case underscores the critical importance of comprehensive endocrine assessment in patients prior to initiating hormone replacement therapy.

Diagnostic Considerations

The clinical, laboratory, and genetic features in this case established the diagnosis of *HLA-A**31:01-associated CBZ-induced DIHS, consistent with the DRESS criteria [1]. The RegiSCAR scoring system formally classifies this as a "definite case" (score = 7, Table 1), based on the constellation of cutaneous findings, systemic symptoms, atypical lymphocytosis, eosinophilia, fever, multiorgan involvement, and the close temporal relation to drug initiation [6].

An atypical feature of this presentation was the absence of HHV-6 reactivation. Classical DIHS is thought to involve a two-stage process with an early drug-allergic phase (2–3 weeks), followed by a late viral reactivation phase [7]. The negative HHV-6 test result in this patient may indicate that severe immune-mediated organ damage can occur during the drug-allergic phase alone, without concurrent viral participation, particularly in *HLA-A**31:01-positive individuals with high-avidity drug-specific CTL responses.

Clinical and Public Health Implications

This case highlights the necessity for increased clinical vigilance in *HLA-A**31:01 carriers who are prescribed CBZ. Preprescription *HLA-A**31:01 testing

Table 1 RegiSCAR Scoring for DIHS/DRESS

RegiSCAR Criteria	This Case	Points
Fever ≥ 38.5°C	Yes (39.0°C documented)	0
Enlarged lymph nodes (≥ 2 sites, > 1 cm)	Yes (cervical and axillary lymphadenopathy > 1 cm)	1
Eosinophilia (≥ 10% or ≥ 700/μL)	Yes (45–60% on days 14–30)*	2
Atypical lymphocytes	Yes (prominent on peripheral blood differential)	1
Skin involvement > 50% BSA	Yes (generalized erythroderma documented)	1
Organ involvement (≥ 2 organs)	Yes (liver, kidney, lung, thyroid, adrenal - 5 organs)	2
Resolution > 15 days	Yes (gradual resolution over several weeks)	0
Exclusion of other causes	Yes (comprehensive infectious/autoimmune workup negative)	0
TOTAL RegiSCAR SCORE		7 points
CLASSIFICATION		Definite DRESS (threshold ≥ 5)

*Note: Eosinophil count was initially 0% on admission but subsequently rose to 45–60% during days 14–30, consistent with the characteristic biphasic pattern observed in DIHS/DRESS. DIHS/DRESS: Drug-induced hypersensitivity syndrome/Drug reaction with eosinophilia and systemic symptoms.

has been demonstrated to be cost-effective even in the Japanese population (£12,808 per quality-adjusted life-year, well below the U.K. threshold for cost-effectiveness) [8]. Current clinical practice guidelines in Japan increasingly recommend pre-prescription HLA genotyping for all patients prior to CBZ initiation.

The rarity of endocrine involvement in DIHS, combined with the potentially life-threatening consequences of undiagnosed adrenal insufficiency, mandates comprehensive endocrine evaluation in all patients with DIHS, including assessment of adrenal function before thyroid hormone or other metabolic therapies are initiated. This case serves as a reminder that DIHS can present with atypical organ involvement and that clinicians must maintain a high index of suspicion for multisystem complications beyond the hepatic, renal, and pulmonary manifestations typically emphasized in the literature.

CONCLUSION

Herein, we report the first case of primary adrenal insufficiency in Japan in the context of CBZ-induced DIHS in an *HLA-A**31:01-positive patient. This case is notable for the occurrence of AIN and primary hypothyroidism in the absence of HHV-6 reactivation. The manifestation of adrenal insufficiency after thyroid hormone replacement underscores the pathophysiological principle that hormone replacement must be approached cautiously in patients with simultaneous multiendocrine dysfunction.

*HLA-A**31:01 carriers represent a high-risk population for severe CBZ-induced adverse reactions, and comprehensive pretreatment genetic screening remains an essential preventive strategy. Close multidisciplinary monitoring, including regular assessment of endocrine, renal, hepatic, and immunological function, is recommended for all patients with suspected DIHS. Future research elucidating the mechanisms of organ-specific T-cell infiltration in DIHS may identify biomarkers that predict which patients will develop rare endocrine complications. Longitudinal follow-up is essential, as endocrine dysfunction following DIHS may represent either permanent gland destruction or potentially reversible immune-mediated injury; in this patient, primary hypothyroidism persisted at 3-month follow-up and adrenal functional recovery has not yet been formally assessed. Furthermore, considering accumulating evidence that DIHS can trigger multi-endocrine autoimmune sequelae through Treg dysfunction [9], systematic and long-term endocrine surveillance — encompassing thyroid function, glucose metabolism, and adrenal reserve — is strongly recommended for all patients following DIHS resolution.

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REFERENCES

1) Kroshinsky D, Cardones AG, Blumenthal KG. Drug Reaction with Eosinophilia and Systemic Symptoms. N Engl J Med. 2024; 391: 2242–54.
2) Drug-induced hypersensitivity syndrome (DIHS) clinical practice guideline 2023. Jpn J Dermatol. 2024; 134(3): 559–580, https://www.dermatol.or.jp/dermatol/wpcontent/uploads/xoops/files/guideline/DIHS2023.pdf
3) McCormack M, Alfirevic A, Bourgeois S, Farrell JJ, Kasperavičiūtė D, Carrington M, *et al*. HLA-A*3101 and carbamazepine-induced hypersensitivity reactions in Europeans. N Engl J Med. 2011; 364(12): 1134–1143.
4) Ozeki T, Mushiroda T, Yowang A, Takahashi A, Kubo M, Shirakata Y, *et al*. Genome-wide association study identifies HLA-A*3101 allele as a genetic risk factor for carbamazepine-induced cutaneous adverse drug reactions in Japanese population. Hum Mol Genet. 2011; 20(5): 1034–1041.
5) Pirmohamed M, Ostrov DA, Park BK. New genetic findings lead the way to a better understanding of fundamental mechanisms of drug hypersensitivity. J Allergy Clin Immunol. 2015; 136(2): 236–244.
6) Kardaun SH, Sekula P, Valeyrie-Allanore L, Liss Y, Chu CY, Creamer D, *et al*. Drug reaction with eosinophilia and systemic symptoms (DRESS): an original multisystem adverse drug reaction. Results from the prospective RegiSCAR study. Br J Dermatol. 2013; 169(5): 1071–1080.
7) Husain Z, Reddy BY, Schwartz RA. DRESS syndrome: Part I. Clinical perspectives. J Am Acad Dermatol. 2013; 68: 693. e1–14.
8) Plumpton CO, Yip VLM, Alfirevic A, Marson AG, Pirmohamed M, Hughes DA. Cost-effectiveness of screening for HLA-A*31:01 prior to initiation of Carbamazepine in epilepsy. Epilepsia. 2015; 56(4): 556–563.
9) Deng M, Wu H, Yu M, Tian Y, Li Y, Xiao X. Co-Occurrence of Multiple Endocrine Abnormalities Induced by the DIHS/

DRESS. Int J Endocrinol. 2019; 2019: 7959615. https://doi.org/10.1155/2019/7959615
10) Tempark T, Deekajorndech T, Chatproedprai S, Supornsilchai V, Wananukul S. Late sequelae of drug reaction with eosinophilia and systemic symptoms (DRESS) cause thyroid dysfunction and thyroiditis: review of literature. J Pediatr Endocrinol Metab. 2022; 35(5): 567–575. doi: 10.1515/jpem-2021-0685.6