Int J Clin Exp Med 2023;16(10):235-242
www.ijcem.com /ISSN:1940-5901/IJCEM0152201

Case Report

Sheehan syndrome complicated with coronary heart disease: a report of 2 cases

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Received July 13, 2023; Accepted September 18, 2023; Epub October 15, 2023; Published October 30, 2023

Abstract: Background: Sheehan syndrome, a type of hypopituitarism ensuing from postpartum hemorrhage, seldom manifests concomitantly with coronary atherosclerotic heart disease. The gestational period witnesses an augmentation in the pituitary gland's size, thereby escalating its oxygen requirements and rendering it more susceptible to hypoxic conditions. An acute, substantial hemorrhage during childbirth can precipitate ischemic necrosis in the anterior pituitary cells. This results in a marked decline in the secretion of its array of hormones, culminating in the degeneration of their respective target organs and the onset of multifarious symptomatic manifestations. Case presentation: We delineate two distinct cases of Sheehan syndrome conjoined with coronary atherosclerotic heart disease. In the first case, the patient, having a medical background of postpartum hemorrhage and percutaneous coronary intervention, presented with precordial and dorsal pain. Laboratory investigations indicated aberrantly elevated myocardial damage markers. Acute coronary syndrome was diagnosed upon admission. Further assessments, comprising pituitary hormone levels and MRI, unveiled pituitary atrophy (termed as "empty sella"), attenuated thyroid-stimulating hormone, and adrenocorticotropic hormone levels. A conclusive diagnosis of Sheehan syndrome was then ascertained. Following a regimen of hormone replacement therapy, the patient's physiological state attained stability. The second case involved a patient previously diagnosed with Sheehan syndrome, who exhibited symptoms such as chest constriction, dorsal discomfort, and transient syncope-induced fatigue. Acute coronary syndrome was diagnosed upon her admission. A subsequent comprehensive assessment, encompassing coronary angiography and cardiac MRI, revealed her afflictions to be variant angina pectoris and acquired QT prolongation syndrome. A subsequent course of hormone replacement therapy stabilized the patient's condition. Conclusion: Hypopituitarism, resulting from Sheehan syndrome, compromises central hormonal secretion, and the concomitant deficiency of multiple pituitary hormones can often obscure clinical manifestations, leading to potential diagnostic oversight. The resultant hypothyroidism can induce rhabdomyolysis, which could erroneously be diagnosed as an acute myocardial infarction and may predispose individuals to a spectrum of cardiovascular pathologies.

Keywords: Sheehan syndrome, coronary atherosclerotic heart disease, hypothyroidism, variant angina, acquired long QT syndrome

Introduction

Sheehan syndrome, an unusual hypopituitarism secondary to significant postpartum hemorrhage, is infrequently encountered in both endocrinology and obstetrics. Its coexistence with coronary heart disease is even scarcer. A meticulous search of the CNKI database using the terms "Sheehan syndrome" and "coronary heart disease" yielded no analogous case reports. Conversely, the PubMed database showed a mere two reports concerning pituitary-related myocardial infarction [1, 2]. The challenge lies in diagnosing Sheehan syndrome amidst treatment for coronary heart disease, or in instances where coronary atherosclerosis progresses unchecked due to hypothyroidism concomitant with Sheehan syndrome. To elucidate the coronary heart disease etiology rooted in Sheehan syndrome and to aid accurate diagnosis and clinical management, we detail two illustrative cases.

Case presentation

Case 1

A female patient, 58 years of age, presented with a medical history remarkable for massive hemorrhage during childbirth 27 years prior. This event was accompanied by postpartum agalactia, amenorrhea, and chronic anemia, yet it was largely overlooked. She had been diagnosed with hyperlipidemia eight months prior and had been managed with oral atorvastatin calcium tablets (20 mg nightly). Additionally, she had a one-month history of hypertension, with peak readings of 160/90 mmHg, treated with oral enalapril maleate (5 mg daily).

Eight months before the current admission, she began experiencing palpitations. Coronary angiography revealed non-significant stenosis in the LM and LCX, but displayed pronounced stenosis in the proximal and mid-segments of LAD (with a maximum of 90%), ostial stenosis in D1 (90%), and diffuse stenosis in the central segment of RCA (90%). Consequently, she underwent percutaneous coronary interventions in LAD and RCA. Post-operation, she was prescribed an oral regimen of "Aspirin 100 mg once per night, Ticagrelor 90 mg twice per day, and Atorvastatin Calcium Tablets 20 mg once per night".

Twelve hours prior to her most recent admission, she reported recurrent bouts of chest and dorsal pain, accompanied by asphyxia, dyspnea, and excessive perspiration. Each episode persisted for approximately 20 minutes, prompting her visit to our emergency department. Diagnostic evaluations included: ECG which exhibited sinus rhythm with diminished limb lead voltage and multiple low T-waves; Chest CT showcasing bilateral pulmonary interstitial alterations; and a cardiac ultrasound identifying left atrial dilation, moderate mitral regurgitation, minor tricuspid regurgitation, and an absence of segmental wall motion anomalies. Laboratory analysis revealed the following: Myocardial injury markers such as CK-MB at 34.16 ng/mL (0-2.03 ng/mL), myoglobin at 218.3 ng/mL (0-61.5 ng/mL), and cardiac troponin I < 0.01 ng/mL (0.000-0.034 ng/mL); Hemoglobin at 100 g/L (115-150 g/L). Physical examination findings were as follows: body temperature at 36.7°C, pulse rate of 65 beats/min, respiratory rate of 19 breaths/min, blood pressure of 113/65 mmHg, a notably lethargic response, diminished facial expressions, sparseness of eyebrows, absence of axillary and pubic hair, a diminished cardiac boundary, heart rate at 65 beats/min, and the absence of pathological murmurs across valve auscultation zones. Subsequent laboratory evaluations post-hospitalization indicated myocardial injury markers: CK-MB at 7.53 ng/mL (0-2.03 ng/mL), myoglobin at 82.4 ng/mL (0-61.5 ng/mL), and cardiac troponin I at 0.012 ng/mL (0.000-0.034 ng/mL). Lipid profiles revealed very low density lipoprotein cholesterol at 0.84 mmol/L (0.00-0.76 mmol/L), lipoprotein(a) at 333 mg/L (0-300 mg/L), triglycerides at 2.11 mmol/L (< 1.70 mmol/L), high density lipoprotein at 0.76 mmol/L (1.04-1.55 mmol/L), and low density lipoprotein cholesterol at 3.05 mmol/L (1.89-3.37 mmol/L). Serum enzyme levels were as follows: creatine kinase at 2389 U/L (40-200 U/L), α-Hydroxybutyrate dehydrogenase at 376 U/L (72-182 U/L), lactate dehydrogenase at 504 U/L (120-250 U/L), creatine kinase isoenzyme at 27.10 ng/mL (0.60-6.30 ng/mL), and aspartate aminotransferase at 76 U/L (13-35 U/L).

Assessment of six pituitary hormones yielded: thyroid-stimulating hormone at 2.480 μIU/mL (0.27-4.2 μIU/mL), adrenocorticotropic hormone at 6.29 pg/mL (08:00-10:00 AM, 6.0-40 pg/mL), growth hormone at 0.08 ng/mL (0.06-5 ng/mL), luteinizing hormone at 0.99 mIU/mL (menopause, 7.7-58.5 mIU/mL), prolactin at 6.14 ng/mL (4.79-23.3 ng/mL), and follicle-stimulating hormone at 1.94 mIU/mL (menopause, 25.8-134.8 mIU/mL). Thyroid function metrics were as follows: thyroid-stimulating hormone at 2.630 μIU/mL (0.27-4.2 μIU/mL), free triiodothyronine at 1.81 pg/mL (2.0-4.4 pg/mL), free thyroxine at 0.37 ng/dl (0.93-1.7 ng/dl), and triiodothyronine at 0.67 ng/mL (0.8-2.0 ng/mL). A bilateral adrenal CT appeared normal. Notably, pituitary MRI displayed pituitary atrophy, exemplified by the empty Sella (**Figure 1**). Given the historical context of postpartum hemorrhage, the unequivocal diagnosis was Sheehan syndrome. Management comprised of Levothyroxine Sodium Tablets (25 μg daily) and Prednisone Acetate (5 mg daily) as hormone replacement therapy. Subsequent to the initiation of hormone replacement therapy, the patient displayed marked improvements in appetite and responsiveness.

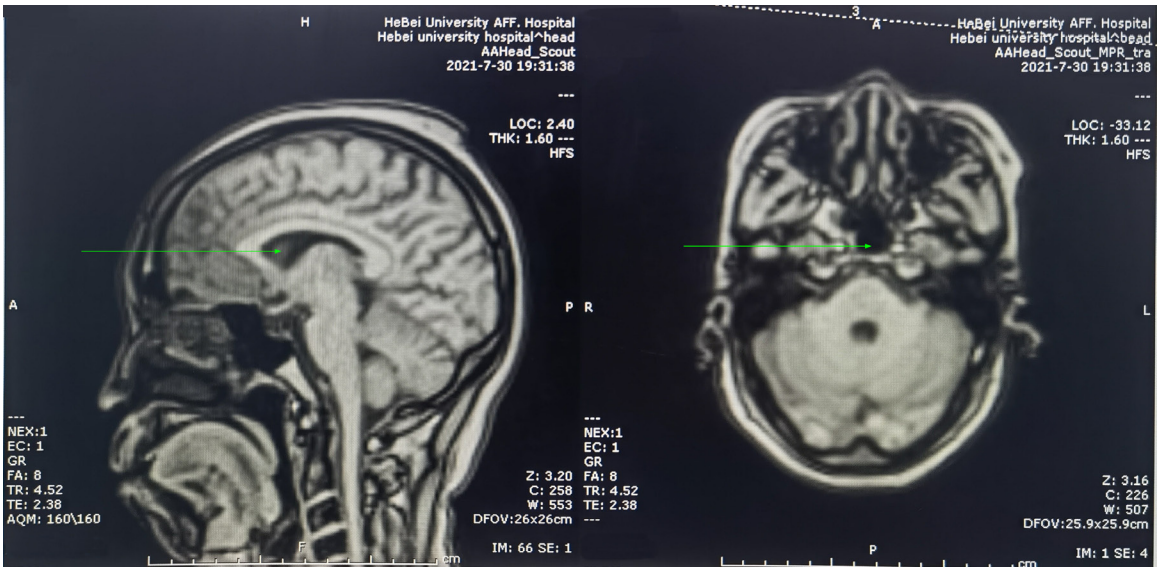

Figure 1. Pituitary MRI revealed pituitary atrophy, which manifested as an empty sella (green arrow indication).

Following comprehensive electrolyte rebalancing, intensive lipid reduction, and amelioration of myocardial ischemia, the patient's clinical status was deemed stable.

Case 2

A 41-year-old Chinese female presented with a significant medical history of profuse hemorrhage during a cesarean section 13 years prior, culminating in a diagnosis of Sheehan syndrome. Her therapeutic regimen included intermittent oral levothyroxine sodium at a dose of 25 μg daily.

In the eleven hours preceding her hospitalization, she manifested recurrent episodes of chest constriction, dorsal pain, and profound fatigue, devoid of any discernible provocation. These symptoms oscillated in intensity, with periods of reprieve following rest. Merely three hours before her presentation to our facility, she sought medical attention at a local institution due to exacerbated chest discomfort and dorsal pain, during which she experienced a transient episode of syncope. An ECG delineated a sinus rhythm, an elongated QT interval, T wave inversion spanning leads v1-v6, recurrent ventricular premature contractions, and sporadic ventricular tachycardia (illustrated in **Figure 2**). Subsequent to receiving an oral dose of Aspirin (300 mg) and Clopidogrel (300 mg) at the aforementioned facility, she was immediately transferred to our institution.

Upon her arrival to our emergency department, an ECG highlighted a sinus rhythm with T wave inversion in leads v1-v6. Cardiac echography discerned anomalies in the motion of the anterior septal and anterior walls, with a left ventricular ejection fraction (LVEF) documented at 56%. Pulmonary radiographic assessment elucidated bilateral interstitial modifications. Comprehensive laboratory evaluations, encompassing myocardial injury biomarkers, BNP, D-dimer, complete hematological profile, coagulation panel, renal function, electrolytes, and glycemic levels, predominantly returned within standard limits. She was subsequently diagnosed with and managed for acute coronary syndrome.

A thorough physical assessment revealed the following parameters: core temperature of 36.5°C, pulse at 72 beats/min, respiratory frequency of 18 breaths/min, and blood pressure registering 124/73 mmHg. Clinically, she exhibited sparse axillary and pubic hair, an indistinct cardiac silhouette, and an absence of pathological murmurs across all valvular auscultatory points.

Upon post-hospitalization assessment, both myocardial injury markers and D-dimer values were within normal parameters. NT-proBNP was measured at 539 pg/mL (0-300 pg/mL). Thyroid panel results were as follows: triiodothyronine (T3) at 0.37 ng/mL (0.8-2.0 ng/mL), thyroxine (T4) at 0.93 μg/dL (5.1-14.1 μg/dL),

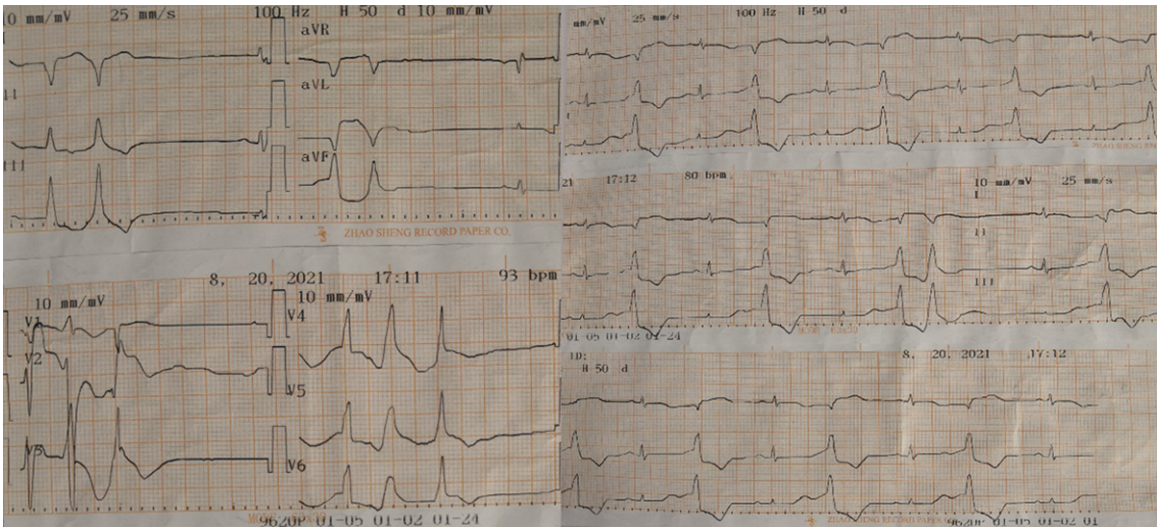

Figure 2. The patient's ECG was examined in a nearby hospital after onset, showed sinus rhythm, prolonged QT interval, T wave inversion in leads v1-v6, recurrent ventricular premature contractions, and sporadic ventricular tachycardia.

free triiodothyronine (FT3) at 1.36 pg/mL (2.0-4.4 pg/mL), free thyroxine (FT4) at 0.12 ng/dL (0.93-1.7 ng/dl), and thyroid-stimulating hormone (TSH) at 0.652 μIU/mL (0.27-4.2 μIU/mL). Lipid profile indicated: triglycerides at 4.70 mmol/L (< 1.70 mmol/L), high-density lipoprotein cholesterol (HDL-C) at 0.88 mmol/L (1.04-1.55 mmol/L), and low-density lipoprotein cholesterol (LDL-C) at 2.54 mmol/L (1.89-3.37 mmol/L). Serum enzyme analysis showed creatine kinase levels at 322 U/L (40-200 U/L).

Coronary angiographic evaluation revealed an absence of notable coronary stenosis, though it did indicate decelerated coronary blood flow. A subsequent cardiac magnetic resonance imaging (MRI) displayed no discernable irregularities. Based on these findings, a clinical diagnosis of variant angina pectoris was determined. The therapeutic protocol comprised oral Nicorandil Tablets at a dosage of 5 mg three times per day.

Assessment of the pituitary panel revealed: adrenocorticotropic hormone (ACTH) at 6.06 pg/mL (08:00-10:00 AM, 6.0-40 pg/mL), follicle-stimulating hormone (FSH) at 0.89 mIU/mL (menopause, 25.8-134.8 mIU/mL), growth hormone (GH) at 0.05 ng/mL (0.06-5 ng/mL), luteinizing hormone (LH) at 0.73 mIU/mL (menopause, 7.7-58.5 mIU/mL), prolactin at 3.69 ng/mL (4.79-23.3 ng/mL), and TSH at 0.752 μIU/mL (0.27-4.2 μIU/mL).

Endocrine panel measurements included: ACTH at 6.04 pg/mL (08:00-10:00 AM, 6.0-40 pg/mL), estradiol at 5.00 pg/mL (5-138 pg/mL), FSH at 0.94 mIU/mL (menopause, 25.8-134.8 mIU/mL), GH at 0.05 ng/mL (0.06-5 ng/mL), LH at 0.72 mIU/mL (menopause, 7.7-58.5 mIU/mL), prolactin at 3.78 ng/mL (4.79-23.3 ng/mL), progesterone at 0.05 ng/mL (0.05-0.1 ng/mL), testosterone at 0.03 ng/mL (0.03-0.481 ng/mL), and TSH at 0.799 μIU/mL (0.27-4.2 μIU/mL).

Cortisol evaluations were documented with cosyntropin at 0.63 pg/mL (08:00-10:00 AM, 6.0-40 pg/mL) and cortisol at 26.73 ng/mL (20.2-131 ng/mL). Therapeutically, the patient was prescribed Levothyroxine Sodium Tablets 25 μg daily in tandem with Prednisone Acetate 5 mg daily.

Post-therapeutic thyroid panel evaluations revealed: T3 at 0.34 ng/mL (0.8-2.0 ng/mL), T4 at 1.83 μg/dL (5.1-14.1 μg/dL), FT3 at 1.06 pg/mL (2.0-4.4 pg/mL), FT4 at 0.23 ng/dL (0.93-1.7 ng/dL), and TSH at 0.693 μIU/mL (0.27-4.2 μIU/mL). Furthermore, cortisol levels post-treatment were documented with cosyntropin at 5.11 pg/mL (08:00-10:00 AM, 6.0-40 pg/mL) and cortisol at 34.27 ng/mL (20.2-131 ng/mL).

Post-treatment, the patient exhibited clinical stability, with the ECG delineating substantial

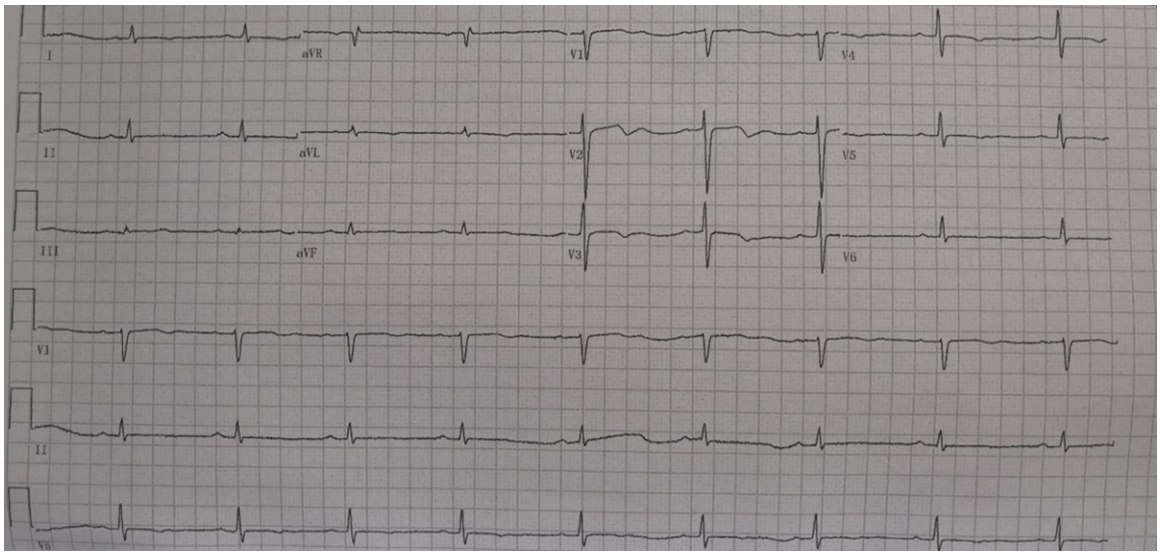

Figure 3. The ECG was reexamined after treatment, which was significantly improved compared with that at the onset.

enhancements compared to previous records (refer to **Figure 3**). The patient was subsequently counseled on the imperative nature of consistent medication adherence and the necessity of periodic medical follow-ups.

Discussion

Sheehan syndrome is delineated by its origin subsequent to postpartum hemorrhage. This is predominantly attributed to prolonged hemorrhagic shock, culminating in hypoxia, degeneration, and eventual necrosis of the anterior pituitary tissue. This cascade of events engenders fibrosis and culminates in pituitary dysfunction, or hypophysis. Fundamentally, this condition manifests as a diminished secretion of pituitary hormones due to compromised functionality of the anterior pituitary. An ensemble of research has unequivocally demonstrated that pituitary dysfunction augments the morbidity and mortality linked with cardiovascular pathologies [3, 4]. Intrinsically, there exists a substantial correlation between hypothyroidism and cardiovascular maladies. Thyroid dysfunction, for instance, has been identified as a precursor to circadian rhythm aberrations [5] and has a pronounced propensity to amplify the risk metrics encompassing obesity, diabetes, and cardiovascular disorders [6]. Furthermore, hypothyroidism potentially catalyzes the progression of coronary atherosclerosis via mechanisms such as the induction of hypercholesterolemia [7, 8], hypertension [9], and endothelial trauma [10]. A salient clinical observation is that individuals with hypothyroidism are predisposed to ventricular irregularities, including torsades de pointes or varying degrees of atrioventricular blocks, which can be attributed to heightened ventricular excitability [11] and extended QT intervals ensuing from prolonged ventricular action potentials [12].

Upon meticulous examination of our index case, it was discerned that the patient's hypothyroidism, resultant from Sheehan syndrome, engendered a reduced metabolic rate and sequentially exacerbated coronary atherosclerosis. This inference was drawn based on the patient's comprehensive medical chronicle, physical assessment, pituitary hormonal evaluations, and magnetic resonance imaging of the pituitary. Subsequent reevaluations indicated that despite elevated cardiac troponin I, significant surges in serum enzyme creatine kinase were observed. This, coupled with a noticeable imbalance in the ratios of creatine kinase isoenzyme, α-hydroxybutyrate acid dehydrogenase, and lactate dehydrogenase, and the absence of dynamic ST-segment alterations in the ECG, led to the hypothesis that the patient's chest and dorsal discomforts, which mitigated post hormone replacement therapy, did not align with an acute myocardial infarction diagnosis. A plausible explanation for

the pronounced increment in creatine kinase is its association with rhabdomyolysis, secondary to hypothyroidism [13, 14]. It's imperative to underscore that this patient met the diagnostic criteria for Sheehan syndrome 27 years prior. However, the perennial belief, borne out of her postpartum hemorrhage experience, was a perceived intrinsic weakness, evidenced by her amenorrhea and absence of lactation. Intriguingly, even her percutaneous coronary intervention, conducted eight months prior, failed to elicit due diligence from both the patient and the attending physician. This oversight may be attributed to the concurrent presence of multiple pituitary hormone deficiencies, which paradoxically obfuscate distinct clinical symptoms, rendering them imperceptible. For instance, the quintessential manifestations of hypothyroidism, notably cold intolerance and weight accrual, are counterbalanced by the vasomotor symptoms associated with hypogonadism and weight attenuation resulting from adrenocortical insufficiency. An assiduous patient history complemented by judicious test selection is pivotal in curtailing misdiagnoses and overlooked diagnoses pertinent to Sheehan syndrome.

In the subsequent case, the patient was swiftly diagnosed with Sheehan syndrome following a severe hemorrhage experienced 13 years prior. Regrettably, despite medical counsel, the patient neither adhered to the daily oral Levothyroxine Sodium regimen (25 μg) nor underwent periodic hormonal evaluations and medication adjustments. This oversight rendered the patient susceptible to undiagnosed hypothyroidism and adrenocortical insufficiency. Presenting with cardinal symptoms such as thoracic constriction, dorsal discomfort, and fatigue - coupled with ECG anomalies like T wave inversions and arrhythmic manifestations - the preliminary diagnosis was acute coronary syndrome. However, following an angiographic assessment revealing insignificant coronary artery stenosis and successive evaluations failing to indicate myocardial injury, acute myocardial infarction was conclusively ruled out. Cardiac MRI further negated any cardiac structural or functional aberrations and myocardial fibrosis, culminating in a diagnosis of variant angina. Two salient links between the inception of variant angina pectoris and patient hypothyroidism were identified: (1) thyroid hormone insufficiency impacting β-receptor coupling to adenylyl cyclase, thereby enhancing coronary artery spasm susceptibility due to reduced α-receptor antagonism [15]. And (2) vascular endothelial malfunctions due to hypothyroidism escalating vasoconstrictors, subsequently inducing coronary artery spasms [16].

The patient's syncope episodes could potentially be attributed to: 1. Acquired QT prolongation syndrome, a collection of syndromes manifested by ECG-observed QT prolongation, arrhythmias, syncope, and sudden mortality. Given the absence of any pertinent familial history, cardiac structural anomalies, electrolyte imbalances, or QT-prolonging medication, the primary etiology of this QT prolongation was plausibly hypothyroidism, a sequela of Sheehan syndrome. 2. Variant angina-induced syncope, with chest discomfort being the paramount symptom occasionally concurrent with or manifesting solely as syncope [17]. Furthermore, spasms in the right coronary artery are observed to be more conducive to syncope than those in the left anterior descending artery [18].

Remarkably, even with a prior diagnosis of Sheehan syndrome, the patient's condition was reminiscent of the first case due to similar neglect. This underscores the contention that many individuals may inadvertently overlook the manifestations of Sheehan syndrome, either due to the antagonistic effects of hormonal imbalances or by forgoing regular pituitary hormonal assessments and medication adjustments despite undergoing hormone replacement therapy.

It is imperative to highlight findings from a comprehensive prospective investigation indicating that hypopituitarism may amplify cardiovascular mortality via growth hormone deficiency [19]. Moreover, gonadotropin deficiency is postulated to play a pivotal role in the surge of vascular mortality amongst hypopituitary patients [20]. Specific hormone insufficiencies, stemming from hypopituitarism, can profoundly exacerbate the onset and progression of cardiovascular maladies.

Conclusion

Within this manuscript, we elucidate two uncommon presentations of Sheehan syndrome

concomitant with coronary heart disease. Due to the inherent nature of hypopituitarism, where diminished central hormonal secretion occurs, a plethora of concurrent pituitary hormonal deficiencies can inadvertently mask the characteristic clinical symptoms of hormonal insufficiency, rendering the diagnosis elusive. Concurrently, rhabdomyolysis, a consequence of hypothyroidism, positions patients at a heightened risk of erroneous diagnosis, particularly being mistaken for acute myocardial infarction. It is imperative to underscore that hypothyroidism, secondary to Sheehan syndrome, not only predisposes individuals to rhabdomyolysis but also catalyzes the onset of an array of cardiovascular pathologies. Early detection, paired with judicious hormone replacement therapy and rigorous patient monitoring during medication courses, is pivotal for the efficacious prevention and management of associated cardiovascular complications.

Acknowledgements

These case reports were supported by doctors working in the Department of Cardiology, Affiliated Hospital of Hebei University in acquisition, analysis, and interpretation of data.

Written informed consent was obtained from the patients.

Disclosure of conflict of interest

None.

Abbreviations

ECG, Electrocardiogram; MRI, Magnetic Resonance Imaging.

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References

[1] Gupta V, Patil S, Raval D and Gopani P. Pituitary apoplexy presenting as myocardial infarction. Indian J Endocrinol Metab 2014; 18: 232-233.

[2] Ghosh R, Chatterjee S, Roy D, Dubey S and Lavie CJ. Panhypopituitarism in acute myocardial infarction. Ann Afr Med 2021; 20: 145-149.

[3] Klose M, Marina D, Hartoft-Nielsen ML, Klefter O, Gavan V, Hilsted L, Rasmussen AK and Feldt-Rasmussen U. Central hypothyroidism and its replacement have a significant influence on cardiovascular risk factors in adult hypopituitary patients. J Clin Endocrinol Metab 2013; 98: 3802-3810.

[4] Harbeck B, Haas CS, Suefke S and Moenig H. Cardiovascular risk factors and disease in patients with hypothalamic-pituitary disorders. Int J Cardiol 2015; 184: 464-465.

[5] Ikegami K, Refetoff S, Van Cauter E and Yoshimura T. Interconnection between circadian clocks and thyroid function. Nat Rev Endocrinol 2019; 15: 590-600.

[6] Allada R and Bass J. Circadian mechanisms in medicine. N Engl J Med 2021; 384: 550-561.

[7] Pajek M, Avbelj Stefanija M, Trebusak Podkrajsek K, Suput Omladic J, Zerjav Tansek M, Battelino T and Groselj U. Hypercholesterolemia in two siblings with resistance to thyroid hormones due to disease-causing variant in thyroid hormone receptor (THRB) gene. Medicina (Kaunas) 2020; 56: 699.

[8] Kotwal A, Cortes T, Genere N, Hamidi O, Jasim S, Newman CB, Prokop LJ, Murad MH and Alahdab F. Treatment of thyroid dysfunction and serum lipids: a systematic review and meta-analysis. J Clin Endocrinol Metab 2020; 105: dgaa672.

[9] Stabouli S, Papakatsika S and Kotsis V. Hypothyroidism and hypertension. Expert Rev Cardiovasc Ther 2010; 8: 1559-1565.

[10] Sara JD, Zhang M, Gharib H, Lerman LO and Lerman A. Hypothyroidism is associated with coronary endothelial dysfunction in women. J Am Heart Assoc 2015; 4: e002225.

[11] Tribulova N, Knezl V, Shainberg A, Seki S and Soukup T. Thyroid hormones and cardiac arrhythmias. Vascul Pharmacol 2010; 52: 102-112.

[12] Klein I and Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med 2001; 344: 501-509.

[13] Manappallil RG, Muralidharan R, Shalu S and Haneef F. Hashimoto's thyroiditis aggravated by goitrogenic diet presenting as rhabdomyolysis worsened by alcohol intake. BMJ Case Rep 2021; 14: e243385.

[14] Janjua I, Bashir T, Haq MZu, Arshad MF and Sharif M. Severe hypothyroidism presenting with rhabdomyolysis in a young patient. Cureus 2021; 13: e13993.

[15] Cheng CW, Yang NI, Cherng WJ, Hung MJ and Lin KJ. Role of coronary spasm for a positive noninvasive stress test result in angina pecto-

ris patients without hemodynamically significant coronary artery disease. Am J Med Sci 2008; 335: 354-362.
[16] Hubert A, Seitz A, Pereyra VM, Bekeredjian R, Sechtem U and Ong P. Coronary artery spasm: the interplay between endothelial dysfunction and vascular smooth muscle cell hyperreactivity. Eur Cardiol 2020; 15: e12.
[17] Kusama Y, Kodani E, Nakagomi A, Otsuka T, Atarashi H, Kishida H and Mizuno K. Variant angina and coronary artery spasm: the clinical spectrum, pathophysiology, and management. J Nippon Med Sch 2011; 78: 4-12.
[18] Bertrand ME, Lablanche JM, Tilmant PY and Thieuleux FA. Coronary artery spasm. Apropos of 165 cases. Arch Mal Coeur Vaiss 1983; 76: 713-721.
[19] Abs R, Feldt-Rasmussen U, Mattsson AF, Monson JP, Bengtsson BA, Góth MI, Wilton P and Koltowska-Haggstrom M. Determinants of cardiovascular risk in 2589 hypopituitary GH-deficient adults - a KIMS database analysis. Eur J Endocrinol 2006; 155: 79-90.
[20] Tomlinson JW, Holden N, Hills RK, Wheatley K, Clayton RN, Bates AS, Sheppard MC and Stewart PM. Association between premature mortality and hypopituitarism. West Midlands Prospective Hypopituitary Study Group. Lancet 2001; 357: 425-431.