

Spontaneous Hemorrhage of the Thyroid Gland in a Deceased with Hypertensive Emergency Presented with Hemorrhagic Stroke: A Case Report and Literature Review

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Spontaneous intrathyroidal hemorrhage is a rare phenomenon in medicine. Previous reports have described precipitating factors that lead to the condition; however, there is no prior report of the condition in a patient with a hypertensive emergency. The authors presented a case of a deceased 59-year-old male brought to the hospital with loss of consciousness in an episode of hypertensive emergency. The subsequent autopsy revealed hemorrhagic stroke as the cause of death and an incidental finding of intrathyroidal hemorrhage in a thyroid nodule. Further literature review revealed the demographic data as well as the presentation and progression of the patients with the condition. No cases of intrathyroidal hemorrhage and hypertensive emergency have been reported. Airway compression in thyroid hemorrhage can be rapid and fatal. In most cases, surgical intervention is usually required. In cases of spontaneous hemorrhage, there were always thyroid lesions. The present case is an early report of spontaneous intrathyroidal hemorrhage in a hypertensive emergency. Airway protection should be prioritized in case of intrathyroidal hemorrhage. Furthermore, attempt should be made to identify the underlying thyroid pathology. Extensive history taking can also guide attending physicians and pathologists to distinguish between spontaneous and traumatic hemorrhage. In addition, to prevent a fatal consequence, neck examination should also be performed in patients with hypertensive emergency.

Keywords: Thyroid; Hemorrhage; Hypertensive emergency; Hemorrhagic stroke; Intracerebral hemorrhage; Autopsy

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Spontaneous intrathyroidal hemorrhage (SITH) is a rare event^(1,2). There have been case reports on SITH, which were life-threatening, precipitated by various factors⁽³⁻¹⁷⁾. However, it has never been reported in a case of hypertensive emergency, a condition with marked blood pressure (BP) elevations defined as systolic BP greater than 180 mmHg or diastolic BP greater than 110 mmHg with acute target organ damage⁽¹⁸⁾. The authors presented a case of SITH in a patient with hypertensive emergency and

intracerebral hemorrhage (ICH) from a hemorrhagic stroke. To better understand SITH, the authors systematically reviewed previous reports on the condition to investigate its epidemiology and causes, as well as clinical symptoms and progression.

Case Report

A 59-year-old Asian man was brought to the emergency department after being found unconscious, alone, on the sofa in his living room after his wife and his son returned home from work in the evening. He was last seen in a healthy condition in the morning, approximately nine hours prior to being found unconscious. At first contact, emergency technicians measured a BP of 250/130 mmHg. Upon arrival at the emergency department of a government hospital, vital signs were recorded as a BP of 238/118 mmHg, pulse rate of 108 per minute, respiratory rate of 12 per minute, and oxygen saturation of 98%. Computed tomography (CT) scan of the brain (Figure 1) revealed massive ICH in the right temporo-parieto-occipital cerebral hemisphere with intraventricular and pontine

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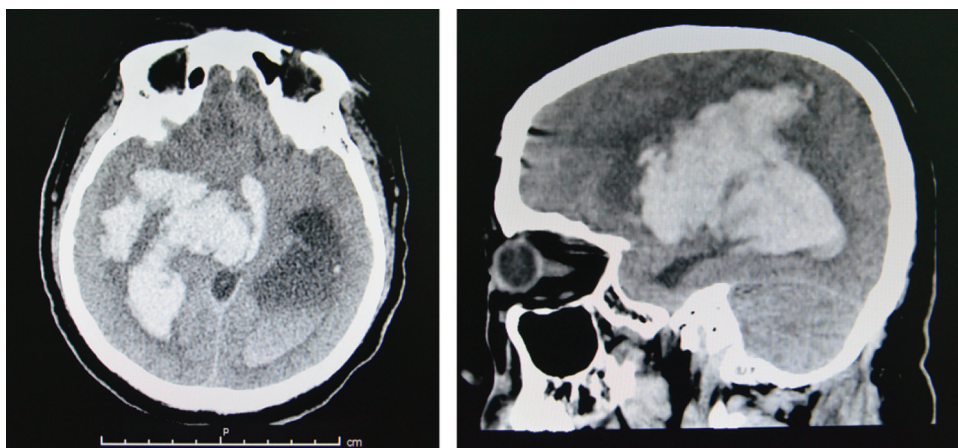


Figure 1. CT scan of the patient at the emergency department showing massive intracerebral and intraventricular hemorrhage.

hemorrhage. These findings confirmed the diagnosis of hypertensive emergency⁽¹⁸⁾. He had been diagnosed with hypertension and type II diabetes mellitus for around 10 years but chose not to receive treatment from healthcare providers, a common practice among Thai patients with non-communicable diseases. He did not have any concurrent medications. No disease of the thyroid gland had been previously diagnosed. His family members also denied any perceivable abnormality of his neck and the deceased did not complain of any symptoms, including headache, neck pain, breathing difficulty, or abnormal swallowing when they last saw him. The patient's condition deteriorated, and he passed away shortly after his arrival. Due to an insurance issue, the body was referred for an autopsy at a medico-legal death investigation center in a university hospital, which has a jurisdiction over the area of his death.

Autopsy findings

The autopsy revealed severe cerebral edema, weighing 1,280 g. ICH was corresponded to the CT scan and was compatible with hemorrhagic stroke. The pontine hemorrhage was secondary to increased intracranial pressure. No evidence of head and neck injuries was found. Neither foreign bodies nor food particles were found in the airway. The autopsy showed signs of long-standing hypertension and diabetes mellitus, including an enlarged heart weighing 450 g, with left ventricular hypertrophy without significant coronary stenosis, and fine granular surfaces of the left and right kidneys, weighing 160 and 140 g, respectively. The liver weighed 1,830 g with a yellow cut surface, compatible with hepatic steatosis. The other organs did not reveal

significant pathological findings.

During the neck dissection, an enlarged cystic thyroid gland was detected. The thyroid gland weighed 80 g, which was significantly heavier than the average weight of thyroid glands of people of the same ethnicity aged 56 to 60 years-old, which was reported as 23 ± 9 g⁽¹⁹⁾. The left thyroid gland alone weighed 70 g and possessed a smooth surface and cystic consistency, measuring $5.0 \times 7.5 \times 4.0$ cm. The cut surface of the left thyroid gland revealed a white, gray encapsulated mass, measuring $3.0 \times 6.5 \times 3.0$ cm, with a firm consistency and central hemorrhage; fresh blood clots almost filled the mass. The right thyroid gland was unremarkable, and there were no signs of tracheal compression. The pathology of the left thyroid gland is shown in Figure 2 and 3.

Serial sections of the left thyroid gland showed a well-defined and encapsulated mass, which was composed of tumor cells in microfollicular and normofollicular patterns without capsular or lymphovascular invasion. A large area of fresh hemorrhage was present. There was no evidence of prior hemorrhages, such as degeneration or hemosiderin-laden macrophages. The histopathological diagnosis was compatible with follicular adenoma (FA). Other significant microscopic findings agreed with the gross pathological findings. Toxicological examinations were negative for ethanol, common substances of abuse, and medications. The cause of death was concluded as hemorrhagic stroke.

Literature review

To identify additional cases with SITH, the authors searched Scopus and PubMed by using the following search terms: "thyroid/thyroidal/

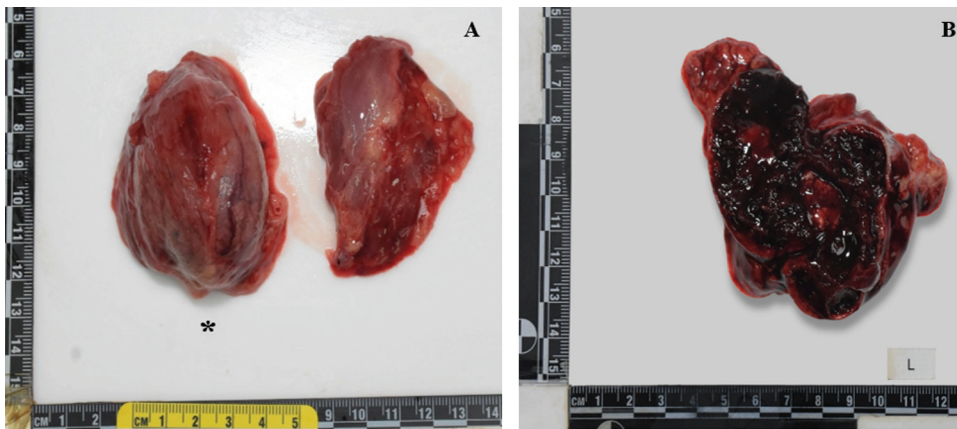


Figure 2. The cystic left (*) versus the right thyroid gland (A) Cut surface of the left thyroid gland with blood clot almost entirely filled the gland (B).

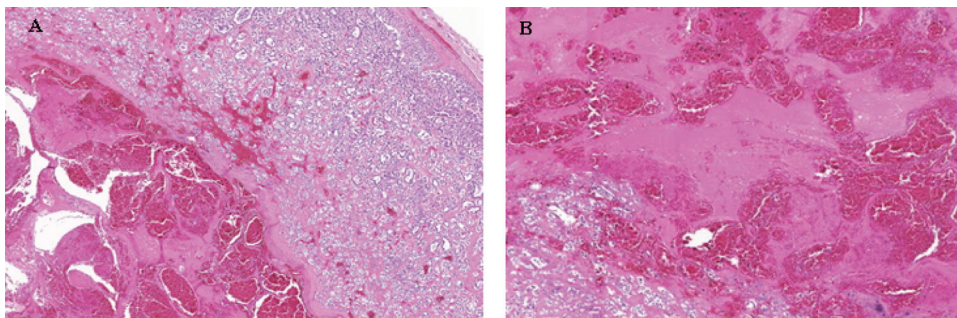


Figure 3. Microscopic findings (H&E staining) of the left thyroid gland with follicular adenoma surrounded by the capsule (A) and the hemorrhagic area (B).

intrathyroidal/intrathyroid/adenoma/goiter” and “hemorrhage/hematoma/bleeding/rupture”. Only articles in English with a clear description of clinical symptoms with radiological or pathological diagnoses of thyroid glands were included. Reports on ectopic thyroid and traumatic thyroid hemorrhage were excluded.

The results of the literature search are chronologically summarized in Table 1⁽²⁰⁻⁴³⁾. The authors retrieved 40 publications with 45 reported cases between 1932 and 2021. Of these 45 cases, 32 (71%) were female. The median age was 64 years, ranging between 3 and 93 years. The number of lesions of the left and right lobes were proportionally similar at 18 versus 13, respectively. Underlying thyroid lesions were found in all cases, with goiter as the most common pathological diagnosis. In 15 cases, precipitating factors for hemorrhage were identifiable, the majority of which included Valsalva maneuver-like activities and antithrombotic agents.

Additionally, the authors investigated patient presentation and progression, which are shown in

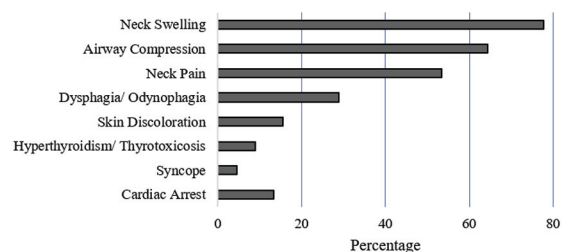


Figure 4. Clinical symptoms and progression of reported cases.

Figure 4 in these 45 cases and discovered that 35 (78%) presented with neck swelling, 29 (64%) with airway compressive symptoms, 24 (53%) with neck pain/discomfort, 13 (29%) with dysphagia/odynophagia, 7 (16%) with ecchymosis/skin discoloration, 4 (9%) with symptoms of thyrotoxicosis of hypertthyroidism, 2 (4%) with syncope, and, most importantly, 6 (13%) patients had a cardiorespiratory arrest. The time of onset of symptoms to the time of diagnosis ranged from a few hours to months.

Of the patients with airway compressive

symptoms, 90% (26 of 29) needed endotracheal intubation or emergency surgery such as hemithyroidectomy, subtotal thyroidectomy, or tracheostomy, to secure the airway. Furthermore, thyroid hormone status was reported in 24 cases, of which 17 (71%) were euthyroid, whereas five (11%) exhibited hyperthyroidism and two (4%) had hypothyroidism.

Discussion

SITH is a rare phenomenon. In two retrospective studies, 59 cases were diagnosed in 631,129 emergency visits (0.009%)⁽¹⁾ and only two cases in 268 patients with functioning thyroid nodules (0.75%)⁽²⁾. From the authors' literature review, we found most cases (71%) were female, and the median age was 64 years. The finding agreed with the epidemiological studies where female and advanced age populations have a higher prevalence of thyroid nodules⁽⁴⁴⁾, and the same reasons that goiter is most reported with SITH as it is the most common type of thyroid nodule⁽⁴⁵⁾.

As shown in Table 1, all cases with SITH, including the present case, had underlying thyroid lesions. This finding contrasts with those of traumatic hemorrhage, in which 42% of cases did not have pre-existing thyroid diseases⁽⁴⁶⁾. The proposed role of thyroid nodules in SITH is the development of vascular abnormalities within them, including fragile vascular structures and the arteriovenous shunting of blood under high pressure^(47,48). Coupled with other factors that enhance the possibility of hemorrhage, SITH can occur under these conditions. The most identifiable precipitating factors of SITH are antithrombotic drugs^(5-9,11-13,16) and Valsalva maneuver-like activities, including defecation⁽⁴⁾, choking/coughing/sneezing^(3,10,15,17), and vaginal delivery⁽¹⁴⁾, which temporarily increase BP. Hemodialysis was reported in one case⁽¹³⁾, but the main factors were thought to be platelet defects and heparin. In the present case, without any other possible precipitating factors for SITH, the authors propose that a marked elevation of BP in a hypertensive emergency was the culprit for SITH. The underlying pathological process might be the fragility of newly formed vessels of the tumor, which could predispose the gland to impending hemorrhage. In addition to significantly elevated intravascular pressure, which could put stress on the vessel walls or lead to damages⁽⁴⁹⁾, as seen in the present case and the previous reports^(3,4,10,14,15,17), it finally contributed to SITH in the deceased.

Although hyperthyroidism/thyrototoxicosis has

been reported in five cases due to hormone release from hemorrhagic follicles^(2,5,6,12), most cases (71%) from the literature review were euthyroid. This might be due to the fact that most thyroid nodules are non-functional⁽⁴⁹⁾. Interestingly, both cases of hypothyroidism had secondary malignancy of the thyroid glands^(39,43), which may be explained by the replacement of thyroid tissues with cancerous cells.

Due to the limited space of the neck, once SITH occurs, the enlarged thyroid gland compresses adjacent cervical structures. Hence, the most frequent complaints of patients with SITH were neck swelling in 78%, airway compressive symptoms in 64%, neck pain/discomfort in 53%, and dysphagia/odynophagia in 29%. Skin discoloration could occur because of the blood spread along the soft tissue^(7,15,17) and possible local inflammation⁽⁶⁾. The progression of SITH to cardiac arrest caused by airway obstruction could be rapid^(4,34). Although, no tracheal compression appeared in the present case, the authors' review showed that almost all cases (90%) with airway compressive symptoms required intubation or immediate surgery to secure the airway. Moreover, Lemke et al.⁽⁴⁶⁾ reported that 24% of cases required emergency airway management in traumatic hemorrhage. Therefore, whether traumatic or SITH, thyroid hemorrhage is among the conditions with medical significance where patients can lose their lives from airway compression. Thus, a plan for airway protection should be considered as early as possible. This concern should also be applied to patients with a hypertensive emergency. Although there are no other reports of SITH caused by a hypertensive emergency, if this condition occurred, there may be consequences that can threaten the patients' lives more rapidly than other hypertensive emergency complications. Thus, in cases of hypertensive urgency, neck examination and monitoring are important in physical examination.

As observed in the present case, where FA was incidentally discovered, and as evidenced by the literature review, all cases of SITH have underlying thyroid pathologies. Thus, once a patient is diagnosed with SITH, physicians should further investigate the disease of the thyroid gland, which sometimes turns out to be a malignancy. Since more than half of the cases revealed thyroid gland diseases⁽⁴⁶⁾, this suggestion should also be applied to traumatic patients. Detailed history taking should also be performed by the attending physicians or pathologists to clarify whether the hemorrhage is spontaneous or traumatic in origin, which may have further legal consequences.

Table 1. Summary of the literature review

Study	Sex/ age (years)	Clinical symptoms & progression					Intubation/ surgical decompression	Disease of the thyroid gland	Thyroid function test	Lobe	Precipitating factors for hemorrhage
		Neck swelling	Airway compressive symptoms	Neck pain/ discomfort	Dysphagia/ odynophagia	Skin discoloration of neck or chest					
McGregor & Cornett, 1952 ⁽⁹⁾	F/68	●	●	●	●	●	●				
Wendel, 1936 ⁽⁴⁾	M/54	●	●	●	●	●	●	Colloid adenoma	N/A	R	Choking and coughing
Bodon & Piccoli, 1957 ⁽²⁰⁾	M/55	●	●	●	●	●	●	Fetal adenoma	N/A	N/A	Dehydration
Berens & Easley, 1958 ⁽²¹⁾	F/68	●	●	●	●	●	●	NG	N/A	L	N/A
Hamburger & Taylor, 1979 ⁽²⁾	F/50	●	●	●	●	●	●	Colloid adenoma	N/A	N/A	N/A
	M/43	●	●	●	●	●	●	Hot nodule	↑	L	N/A
	M/43	●	●	●	●	●	●	Hot nodule	↑	R	N/A
Massie et al., 1981 ⁽²²⁾	F/68	●	●	●	●	●	●	Cyst	N/A	N/A	N/A
Kawamura et al., 1984 ⁽²³⁾	F/56	●	●	●	●	●	●	Cyst	≈	R	N/A
	M/69	●	●	●	●	●	●	Cyst	≈	N/A	N/A
	F/36	●	●	●	●	●	●	Nodule	≈	R	N/A
	F/47	●	●	●	●	●	●	Cyst	≈	L	N/A
	F/26	●	●	●	●	●	●	Cyst with calcifications	≈	L	N/A
Olchovsky et al., 1985 ⁽⁹⁾	F/72	●	●	●	●	●	●	Nodule	↑	L	Warfarin
Zafar et al., 1991 ⁽²⁴⁾	F/19	●	●	●	●	●	●	Adenomatous colloid goiter	N/A	N/A	N/A
Ajmanid & Krishna, 1999 ⁽²⁵⁾	F/3	●	●	●	●	●	●	Nodule	N/A	R	N/A
Palani et al., 2002 ⁽²⁶⁾	F/56	●	●	●	●	●	●	Cyst	≈	L	N/A
Onal et al., 2006 ⁽⁸⁾	F/63	●	●	●	●	●	●	MNG	↑	L	Heparin
Tsilchorozidou et al., 2006 ⁽⁷⁾	F/80	●	●	●	●	●	●	MNG	≈	R	Warfarin
Chang et al., 2007 ⁽²⁷⁾	F/79	●	●	●	●	●	●	NG	N/A	L	N/A
Yuzbasoglu et al., 2008 ⁽⁸⁾	M/67	●	●	●	●	●	●	Eggshell calcification	≈	L	Aspirin
Testini et al., 2008 ⁽²⁸⁾	F/42	●	●	●	●	●	●	MNG	≈	R	N/A
Chia, 2008 ⁽⁹⁾	M/59	●	●	●	●	●	●	Goiter	≈	L	rt-PA, heparin, aspirin, and clopidogrel
Mohammad & Wan Din, 2009 ⁽²⁹⁾	F/70	●	●	●	●	●	●	NG	N/A	L	N/A
Lee et al., 2011 ⁽³⁰⁾	M/73	●	●	●	●	●	●	Nodular hyperplasia	N/A	L&R	N/A
Kuo et al., 2011 ⁽³¹⁾	M/44	●	●	●	●	●	●	NG	N/A	L	N/A
Gonakls et al., 2011 ⁽³⁰⁾	M/71	●	●	●	●	●	●	FA	N/A	L	Sneezing
Chan et al., 2012 ⁽³²⁾	F/93	●	●	●	●	●	●	Cyst	N/A	L	N/A
Sutter et al., 2013 ⁽³³⁾	F/86	●	●	●	●	●	●	Nodular hyperplasia	N/A	R	rt-PA
Sahin et al., 2014 ⁽¹³⁾	M/64	●	●	●	●	●	●	Nodule	≈	N/A	Heparin, aspirin, and clopidogrel
Vijapurapu et al., 2014 ⁽³⁴⁾	F/70	●	●	●	●	●	●	MNG	N/A	I	N/A
Vijendren et al., 2014 ⁽³⁵⁾	M/48	●	●	●	●	●	●	Follicular carcinoma	N/A	R&I	N/A
Kokatur et al., 2014 ⁽⁴²⁾	F/73	●	●	●	●	●	●	NG	↑	R	Warfarin
Gallant et al., 2015 ⁽³⁶⁾	F/64	●	●	●	●	●	●	NG	N/A	L	rt-PA
Lei et al., 2016 ⁽³⁵⁾	F/63	●	●	●	●	●	●	MNG	≈	N/A	Platelet delects and heparin
Hristov et al., 2016 ⁽¹⁴⁾	F/36	●	●	●	●	●	●	MNG	≈	L&R	Vaginal delivery
Liang & Liu, 2016 ⁽¹⁵⁾	M/74	●	●	●	●	●	●	FA	N/A	R	Coughing
Besr et al., 2016 ⁽³⁷⁾	F/33	●	●	●	●	●	●	Unascertained due to extensive necrosis	N/A	L	N/A
Al-Khalifa et al., 2016 ⁽³⁸⁾	F/36	●	●	●	●	●	●	Cyst	≈	L	N/A
Gunasekaran et al., 2017 ⁽¹⁶⁾	F/91	●	●	●	●	●	●	MNG	≈	R	Warfarin
Abbassi et al., 2018 ⁽³⁹⁾	M/68	●	●	●	●	●	●	MNG	≈	R	Warfarin
Wang et al., 2018 ⁽¹⁷⁾	F/79	●	●	●	●	●	●	Metastatic renal cell carcinoma	↓	L&R	N/A
dell'Aquila et al., 2019 ⁽⁴⁰⁾	F/81	●	●	●	●	●	●	MNG	N/A	R	Coughing
Petersen et al., 2021 ⁽⁴¹⁾	F/80s	●	●	●	●	●	●	FA	≈	L	N/A
Fauzi et al., 2021 ⁽⁴³⁾	F/22	●	●	●	●	●	●	Nodule	≈	R	N/A
Zhang et al., 2021 ⁽⁴³⁾	F/54	●	●	●	●	●	●	Thyroid langerhans cell histiocytosis	↓	I	N/A

F=female; M=male; Y=yes; N=no; NG=nodular goiter; MNG=multinodular goiter; FA=follicular adenoma; ≈=euthyroid; ↑=hyperthyroidism; ↓=hypothyroidism; ●=thyroid gland; L=left lobe of thyroid gland; R=right lobe of thyroid gland; I=thyroid isthmus; rt-PA=recombinant tissue plasminogen activator; N/A=not reported/not applicable

There are two limitations to the present study. First, since the deceased did not follow up on his underlying conditions with any healthcare providers, the authors could not assess the severity of complications caused by his comorbidities apart from anatomical pathological findings related to hypertension and diabetes mellitus. Moreover, thyroid function test was not performed by emergency physicians and postmortem testing was not available in the authors' institution. Hence, the authors could not determine the thyroid hormone status of the deceased. By accessing the types of his underlying thyroid nodules and the data from the authors' literature review, the authors speculated that his thyroid hormone level was likely not to be hyperthyroidism.

Conclusion

To the authors' knowledge, the present case is the first reported case with SITH and hypertensive emergency who died of ICH. Based on the authors' literature review, SITH is more frequently reported in females and with advanced age, additionally, precipitating factors could sometimes be identified. Moreover, all cases had underlying thyroid lesions, especially goiter. Rapid airway compression can lead to death. Hence, airway management is a prime priority. Once thyroid hemorrhage is diagnosed, the attending physician must make efforts to investigate the underlying thyroid pathology. History should be taken in details to determine the manner of hemorrhage. Moreover, physical examination in the case of hypertensive emergency should also include the neck area to prevent a lethal consequence of SITH.

What is already known on this topic?

Spontaneous hemorrhage of the thyroid gland is a rare event in medicine with potentially fatal outcome. There have been reports on precipitating factors that could lead to the condition. Death could be very rapid from airway compression, which usually requires surgical decompression.

What this study adds?

This is the first report of SITH of the thyroid gland precipitated by hypertensive emergency. Moreover, the literature review summarizes patient characteristics and clinical outcomes. It is suggested that underlying thyroid conditions should be investigated in every case of thyroid hemorrhage. A detailed history taking should also be taken by the attending physicians and pathologists, which

can reveal the etiologies of hemorrhage and may have legal consequences. Furthermore, in patients with hypertensive emergency, clinicians should also closely examine and monitor the patients' necks to prevent the possible morbidity and mortality from SITH.

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Ethical approval

This study was approved by the Institutional Review Board of Faculty of Medicine, Chulalongkorn University (IRB No.0995/64, COE No.066/2021) in accordance with the 1964 Declaration of Helsinki and later amendments or comparable ethical standards.

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No funding was received for conducting the present study.

Conflicts of interest

The authors declare no conflict of interest associated with this manuscript.

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