Malaysian J Pathol 2019; 41(3) : 355 – 358

CASE REPORT

Thyroid storm: Is there a role for thyroid function test?

T. Zaharah T. IBRAHIM[1,2], Subashini C. THAMBIAH[1], Intan Nureslyna SAMSUDIN[1], Alia Nasriana NASURUDDIN [2], Miza Hiryanti ZAKARIA[3]

[1]Department of Pathology, Faculty of Medicine & Health Sciences, Universiti Putra Malaysia, Serdang, Malaysia, [2]Department of Pathology, Hospital Tengku Ampuan Afzan, Kuantan, Pahang, Malaysia and [3]Department of Medicine, Hospital Tengku Ampuan Afzan, Kuantan, Pahang, Malaysia

Abstract

Introduction: Thyroid storm (TS) is an endocrine emergency. Early diagnosis for prompt treatment is essential as it has a high mortality rate. *Case Report*: A 31-year-old lady with underlying hyperthyroidism, dilated cardiomyopathy with severe mitral regurgitation presented with shortness of breath. She was intubated and admitted due to decreasing Glasgow Coma Score. Her blood investigations revealed increased white cell count, raised free thyroxine with suppressed thyroid stimulating hormone, deranged liver, renal and coagulation profiles. As her condition did not improve with initial treatment, plasmapheresis was commenced on day 4. Biochemically, her thyroid function test (TFT) showed improvement; however, she succumbed due to multi-organ failure. *Discussion:* Plasmapheresis is considered in TS if there is no clinical improvement within 24-48 hours of initial treatment. The improvement in patient's TFT post plasmapheresis signifies its role in treating TS. Unfortunately, there was a delay in commencing plasmapheresis due to haemodynamic instability in this patient.

Keywords: thyroid storm, hyperthyroidism, thyroid function test, plasmapheresis

INTRODUCTION

Thyroid storm (TS) is an endocrine emergency.[1] There is no specific laboratory test to confirm the diagnosis; hence clinical assessment is important for prompt treatment as TS has a high mortality rate.[2] This condition is commonly seen in patients with underlying hyperthyroidism, especially Graves' disease. It can be induced by surgery, trauma, infection, acute iodine load or parturition.[3] Besides, poor compliance to anti-thyroid drugs (ATD) may be a precipitating factor.[4] Here we report a patient with TS, who did not respond clinically to the initial treatment but post plasmapheresis, her thyroid function test (TFT) improved.

CASE REPORT

A 31-year-old lady, with underlying hyperthyroidism, dilated cardiomyopathy with severe mitral regurgitation, presented to the emergency department with shortness of breath and low Glasgow Coma Score. She had been unwell for 4 days with an upper respiratory tract infection and was anuric. She was under the medical team follow up on carbimazole and warfarin. However, she was non-compliant to medications and restriction of fluid of 1 litre per day.

She was immediately intubated. Her vital signs were as follows: heart rate 180 bpm, blood pressure 140/75 mmHg, SPO_2 78% (high flow mask) and temperature of 38.7°C. Burch-Wartofsky Point Score (BWPS) was 90 (Table 1). On examination, there were bilateral lung crepitations and pedal oedema. Her blood investigations revealed increased white cell count (WCC), raised free thyroxine (fT4) with suppressed thyroid stimulating hormone (TSH), deranged liver, renal and coagulation profiles (Table 2).

In the intensive care unit (ICU), she was started on intravenous medications: Lasix, Augmentin, hydrocortisone; oral propylthiouracil and Lugol's iodine. As she became haemodynamically unstable, inotrope was added. Bedside echocardiogram revealed dilatation of all four chambers with mitral valve flapping. She was

Address for correspondence: Associate Professor Dr. Subashini Chellappah Thambiah, Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400, UPM Serdang, Selangor, Malaysia. Tel: +603-97692779. Email: *subashini@upm.edu.my*

TABLE 1: The BWPS for diagnosis of thyroid storm[1]

CRITERIA			POINT
Thermoregulatory Dysfunction	Temperature (°C)	37.2-37.7	5
		37.8-38.3	10
		38.4-38.8	15
		38.9-39.3	20
		39.4-39.9	25
		>40.0	30
Cardiovascular	Tachycardia	90-109	5
		110-119	10
		120-129	15
		130-139	20
		>140	25
	Atrial Fibrillation	Absent	0
		Present	10
Congestive Heart Failure	Absent		0
	Mild		5
	Moderate		10
	Severe		15
Gastrointestinal-Hepatic Dysfunction	Manifestation	Absent	0
		Moderate (Diarrhoea, Abdominal Pain, Nausea, Vomiting)	10
		Severe (Jaundice)	20
Central Nervous System Disturbance	Manifestation	Absent	0
		Mild (Agitation)	10
		Moderate (Delirium, Psychosis, Extreme Lethargy)	20
		Severe (Coma, Seizure)	30
Precipitating Event	Status	Absent	0
		Present	10
Interpretation	1. TS	Total score:	>45
	2. Impending TS		25-44
	3. TS Unlikely		<25

diagnosed with TS, precipitated by community-acquired pneumonia (CAP), complicated with fast atrial fibrillation, acute kidney injury (AKI), coagulopathy and liver impairment.

She was then commenced on continuous veno-venous haemofiltration by the nephrology team. The propylthiouracil was withheld in view of transaminitis. Due to poor response to the initial treatment, plasmapheresis was started on day 4 of her admission. Her TFT results showed improvement post procedure. Unfortunately, despite being on maximal inotrope support, patient succumbed due to multi-organ failure (MOF) one day after plasmapheresis.

TABLE 2: Patient's laboratory investigations

	Laboratory Parameters	(Day 1)	(Day 2)	Admission (Day 3)	Post Plasmapheresis (Day 4)	(Day 5)
HAEMATOLOGY						
FBC	Hb (12.0-15.0) g/dL	16.5	15.5	14.3	14.8	13.5
	Platelet (150-400) x10^9/L	177	181	200	100	84
	WCC (4.0-10.0) x10^9/L	16.34	18.34	17.56	14.18	13.49
FBP	Leukoerythroblastic blood film with WCC changes. To consider infection.					
COAG	PT (12.0-14.5) sec	23.4	44.1	27.6	33.7	30.2
	APTT (31.0-43.0) sec	41.6	278.7	45.3	46.0	72.9
	INR (1.0)	2.1	4.7	2.6	2.3	2.9
BIOCHEMISTRY						
RP	Urea (3.5-7.2) mmol/L	9.9	12.4	13.1	9.8	13.5
	Creatinine (50-98) μmol/L	139	221	237	168	266
	Na (136-145) mmol/L	136	135	137	135	144
	K (3.5-5.1) mmol/L	3.8	4.3	4.7	2.8	3.2
LFT	Total bilirubin(3.4-20.5)μmol/L	39.6	56.2	121.8	195.4	179.7
	Total protein (60.0-78.0) g/L	42	51	54	42	39.0
	Albumin (29.0-45.0) g/L	21	26	27	22	20
	ALP (40-150) U/L	47	63	84	112	65
	ALT (<56) U/L	50	218	1292	1543	1106
	AST (5-34) U/L	314	650	2575	1475	903
TFT	TSH (0.55-4.78) mIU/mL	<0.008	-	<0.008	-	<0.008
	fT4(11.5-22.7) pmol/L	17.23	-	32.36	-	15.05
	fT3 (3.5-6.5) pmol/L	11.30	-	8.42	-	6.4
CRP	(<5) mg/L	-	69.5	-	43.2	-
MICROBIOLOGY						
Blood C & S		No Growth				

DISCUSSION

The diagnosis of TS is not straightforward as biomarkers for this purpose have not been established. Hence, the diagnosis is primarily clinical.[2] BWPS proposed in 1993 (Table 1) is used to aid diagnosis of TS where a total score of more than 45 is strongly suggestive of TS.[1] This patient's BWSP was 90.

Pathophysiology

Pathophysiology of TS is not fully understood.[5] It is said to be due to the increase of β1-adrenergic receptors being exposed to raised catecholamines in a state of stress.[3] There are a few hypotheses regarding the pathogenesis of TS. Either there is rapid increase in thyroid hormones, giving rise to an abrupt increase in intracellular availability of free thyroid hormones (fT), or, there is diminished physiological reserve due to intercurrent illness. These two mechanisms will lead to imbalance of the normal thyroid hormone homeostasis. In the first hypothesis, during the state of transient saturation of plasma binding capacity, it is sufficient to increase fT. This could lead to increased transporter-mediated intracellular entry of fT causing hyperthyroidism. In the second hypothesis, there is underlying acute or subacute non-thyroidal illness that precipitates TS. A decoupling of oxidative phosphorylation leads to heightened rate of lipolysis and increased oxygen consumption.[5] In this patient, the underlying hyperthyroidism with non-compliance to ATD precipitated by CAP lead to TS.

Laboratory Investigations (Table 2)

Raised WCC and C-reactive protein (CRP) were consistent with underlying infection. The initial

increased urea and creatinine reflected AKI, supported clinically by anuria. The renal profile worsened from day 1 to 3, improving on day 4 post plasmapheresis but deteriorating again on day 5. The potassium level reduced after plasmapheresis, probably due to the effect of replacement regimen using saline and albumin.[6] Increasing trend of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin indicated hepatocellular injury, which can be attributed to the direct effect of increased thyroid hormones. Liver enzyme metabolism can be induced by thyrotoxicosis, or its derangement can be secondary to cardiac failure with hepatic congestion or hypoperfusion.[3] Worsening derangement of renal and liver profiles with coagulopathy was consistent with impending MOF. TFT showed primary hyperthyroidism with suppressed TSH and raised fT4 and fT3, increasing from day 1 to 3 but decreased post-plasmapheresis.

Management

In the consensus for management of thyroid disorders in Malaysia (2012), the therapies used are specifically directed against the thyroid using ATD including thionamides [propylthiouracil (PTU) or methimazole (MMZ)] to block thyroid hormone synthesis followed by Lugol's iodine to prevent thyroid hormone release. Glucocorticoids are used to reduce T4 to T3 conversion. Rarely practised in Malaysia, plasmapheresis can be done in life threatening cases or in patients with contraindication to thionamides.[2] As recommended by the Japanese Thyroid Association and Japanese Endocrine Society Taskforce Committee, it should be considered if there is no clinical improvement within 24-48 hours of initial treatment.[1] Plasmapheresis removes 5'-monodesiodase that converts T4 to T3, thus reducing T3 amount in the serum.[7] However, in this case, there was a delay in starting plasmapheresis due to haemodynamic instability in this patient. Side effects related to plasmapheresis include transfusion reaction, catheter dysfunction, vasovagal reaction, bleeding, hypocalcaemia, respiratory distress, seizure.[8] This patient did not have any of these side effects but her condition deteriorated due to MOF.

CONCLUSION

This patient was treated conventionally for TS; however, she failed to show improvement. Hence, plasmapheresis was commenced. Biochemically her TFT improved, but because of MOF, she succumbed a day after plasmapheresis. If commenced earlier that is within 24-48 hours after initial treatment,[1] she may have had a better prognosis. Plasmapheresis for TS is rarely done in Malaysia[2] and should be considered as an early treatment option in its management.

ACKNOWLEDGEMENT

The authors would like to thank the Director General of Health for his permission to publish this article.

REFERENCES

1. Satoh T, Isozaki O, Suzuki A, *et al*. Guidelines for the management of thyroid storm from The Japan Thyroid Association and Japan Endocrine Society (First edition). Endocr J. 2016; 63(12): 1025-64.
2. Zainudin S, Hussein Z, Jalaludin MY, *et al*. A Summary of the consensus for the management of thyroid disorders in Malaysia. J ASEAN Fed Endocr Soc. 2012; 27(1): 40-3.
3. Carroll R, Matfin G. Endocrine and metabolic emergencies: thyroid storm. Ther Adv Endocrinol Metab. 2010; 1(3): 139-45.
4. Idrose AM. Acute and emergency care for thyrotoxicosis and thyroid storm. Acute Med Surg. 2015; 2(3): 147-57.
5. Warnock AL, Cooper DS, Burch HB. Life-Threatening Thyrotoxicosis: Thyroid storm and Adverse Effects of Antithyroid Drugs. Endocrine and Metabolic Medical Emergencies: A Clinician's Guide, Second Edition. 2018; 262-83.
6. Ruiz D, Fonseca San Miguel F, González de Molina FJ, Úbeda-Iglesias A, Navas Pérez A, Jannone Forés R. Plasmapheresis and other extracorporeal filtration techniques in critical patients. Med Intensiva. 2017; 41(3): 174-87.
7. Muller C, Perrin P, Faller B, Richter S, Chantrel F. Role of plasma exchange in the thyroid storm. Ther Apher Dial. 2011; 15(6): 522–31.
8. Keklik M, Kaynar L, Yilmaz M, *et al*. The results of therapeutic plasma exchange in patients with severe hyperthyroidism: a retrospective multicentre study. Transfus Apher Sci. 2013; 48(3): 327-30.