

Clinical Criteria for The Diagnosis of Thyroid Crisis Series of Cases from 2010-2017

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Abstract

Background: Patients whom develop thyrotoxic crisis must be timely identified and aggressive treatment should be started to decrease mortality.

Objectives: The objectives of the study were to identify the clinical characteristics of patients that presented with symptoms suggesting *thyrotoxic crisis (TC)* whom were admitted from 2007 to 2017 at the INCMNSZ, according to the modified diagnostic criteria of TC from the *Japan Thyroid Association (JTA)*.

Methods: Data was obtained from a medical registry of patients who had sufficient clinical elements to evaluate the diagnostic criteria proposed by the JTA. Of 88 identified cases, only 19 patients met inclusion criteria to be evaluated.

Results: 19 patients were diagnosed with autoimmune hyperthyroidism, 74% of the cases were female patients, ages 16 to 56 years old. The most frequent cause was lack of adherence to treatment (42%), followed by pneumonia (31.6%). Total thyroidectomy was performed in 52.6% as definitive treatment. All patients met the diagnostic criteria for TC. The most frequent symptoms were tachycardia (100%) and fever (68.4%). Survival rate following treatment was 100%.

Conclusions The use of the modified clinical criteria of the JTA allows promptly identification of patients with TC, with excellent diagnostic precision, which allows to start immediate medical treatment aiming to control hyperthyroidism symptoms and to prepare the patient for definitive treatment. In our series, survival rate was 100%.

Keywords: clinical, criteria, thyroid, crisis.

Introduction

The prevalence of overt hyperthyroidism is 0.5% in the United States. Hyperthyroidism upsurges with aging and is more commonly seen in female patients. Hyperthyroidism incidence is also reported to be higher in iodine-deficient areas than in areas with sufficient iodine. Hyperthyroidism rates have shown substantial reductions after the introduction of universal salt iodization programs [1]. TC incidence in Japan, reports a hospitalization rate of 0.20 per 100,000 patients per year with more than 10% mortality rate. Among hospitalized patients with thyrotoxicosis, the incidence of TC was reported to be of less than 10%.

In our institute, the total number cases with hyperthyroidism diagnosis was approximately 2,273 patients over the last 10 years. TC prevalence was 0.0083%. TC related mortality in patients without treatment ranges from 80% to 100%, however in hyperthyroid patients whom receive treatment, mortality drops drastically to less than 10%. Mortality was more prevalent in patient presenting additional comorbidities including multiple

organ failure, congestive heart failure, respiratory failure, arrhythmias, disseminated intravascular coagulation, gastrointestinal perforation, sepsis, and hypoxic encephalopathy. On this particular matter, the mortality rate in the group with total bilirubin > 3 mg / dL is significantly higher [2]. The ATA (American Thyroid Association) 2016 guidelines defines TC (thyrotoxic crisis) as the presence of signs and symptoms of hyperthyroidism, generally severe, accompanied by variable manifestations of multisystemic organ failure [3]. The analysis of the Burch-Wartofsky Criteria in the diagnosis of TC, led to the suggestion the ATA criteria for TC are difficult to apply in emergent situations due to their complexity. The diagnostic criteria proposed by the Japanese Thyroid Society (JPTS) are eminently clinical and avoid assigning scores to patients with hyperthyroid signs and symptoms. Another point to consider is that not all the cases reach the required score to be consider TC, however clinically they have strong features to consider TC as a diagnosis. Both guidelines ATA and JPTS could misclassify some cases, hence it should always be

considered that a patient with severe hyperthyroidism with multiorgan findings is developing or already has thyroid crisis. Patients with a Burch-Wartofsky score ≥ 45 classified as TC 1 or TC2 category from the Japan Thyroid Association (AJT) require aggressive therapy. The decision to use aggressive therapy in Patients with a Wartofsky score between 25 and 44 should be based on clinical judgment. A multimodal treatment approach for patients with TC should be used, including beta-adrenergic blockade, antithyroid drug therapy, inorganic iodine, corticosteroid therapy, acetaminophen, volume replacement, nutritional support, respiratory care and monitoring in an intensive care unit, individualizing each case.

Materials and Methods

We present a retrospective study, records were reviewed from 2007 to 2017 at the INCMNSZ, only TC cases were selected. We found 80 patients in our archival database with a diagnosis of TC, only 19 patients met the criteria for TC according to the criteria of the Japanese Thyroid Association. Demographic information included sex, age, origin, level of education. Clinical information incorporated

to our data base included: family history of previous autoimmune thyroid diseases, hyperthyroidism as initial presentation upon ER admission, medical treatment prior to their admission, possible precipitating triggers for TC. We analyzed laboratory data including: kidney function tests, liver function tests, thyroid function tests. Finally, we reviewed the medical treatment given during hospital admission.

Statistical analysis: Descriptive study, the categorical variables were analyzed and presented in frequency tables.

Results

The criteria proposed by the AJT include, as a prerequisite for TC diagnosis, is biochemical determinations of elevated free hormones; unfortunately, since we were not able to retrieve such determinations, we would classify our cases as suspected diagnosis of TC (CT2).

One of the proposals of our study, is to consider including an index based on the values of total hormones TT3 / TT4 as a biochemical indication of excess thyroid hormones or the calculated free thyroxine index.

Table I: Demographic characteristics patient admitted with CT (2007-2017) at the INCMNSZ.

	Total patients (19)	Percentage (%)
Gender		
-Man	5	26.3
- Woman	14	73.7
Age (years)	32 (16-56)	
City		
-CDMX	13	68.4
-Estado de México	4	21.1
-Hidalgo	1	5.3
-Puebla	1	5.3
Education level		
-Primary	4	21.2
-High school	11	57.9
-Higher	3	15.8
-None	1	5.3
Admission Diagnosis		
-Graves' disease	11	57.9
-Autoimmune hyperthyroidism	8	42.10%
	Total patients (19)	Porcentaje (%)
Etiology		
-Medication non compliance	8	42.1%
-Pneumonia	6	31.6%
-Post radioactive iodine	1	5.3%
-Intestinal infection	2	10.5%
-Urinary tract infection	2	10.5%
Methimazole induced Agranulocytosis	3	15.8%
Definitive treatment		
Registration request	1	5.3%
B / R	2	10.6%
ATM	5	26.3%
TT	10	52.6%
Radioactive iodine		

B/R: Block- Replace; ATM: Antithyroid medication; TT: Total thyroidectomy

The diagnostic criteria according to the AJT as described in Table II.

TABLE II: Classification according to the AJT for CT in INCMNSZ patients from 2007-2017.

	Total patients (19)	Percentage (%)
SYMPTOM		
1. CNS: drowsy, Glasgow <14 and agitation.	11	57.9%
2. FEVER:> 38 ° C	13	68.4%
3. HR> 130 bpm	19	100%
4. CHF: rales in 2/3 of both lung fields.	7	36.8%
5. GASTROINTESTINAL: nausea, vomiting and diarrhea.	7	36.8%
LIVER: jaundice with bilirubin> 3mg / dl	3	15.78%
DIAGNOSIS		
CT 1 definid	3	15.78%
CT 2 suspect	16	84.21%
CNS: Central Nervous System; HR: heart rate; CHF: Congestive Heart Failure. CT: thyrotoxic crisis according to the AJT.		

TABLA III: Laboratory findings in patients with TC from 2007-2017 at INCMNSZ

	Reference ranges	Results	Number of patients (%)
Creatinine mg/dl	0.6-1.2	0.18-0.59	15(78.94%)
		0.6-1.2	4 (21.05%)
Alkaline phosphatase U/L	34-104	34-104	1 (5.26%)
		105-188	9 (47.36%)
		225-398	6 (31.57%)
		417-427	3 (15.78%)
Magnesium mg/dl	1.9-2.7	1.2-1.8	16(84.21%)
		1-9-2.1	3 (15.78%)
Total bilirubin mg/dl	0.3-1	0.3-1	7 (36.84%)
		1.10-1.6	7 (36.84%)
		2.4-3.38	3(15.78%)
		5-18.1	2 (10.5%)
Direct bilirubin mg/dl	0.03-0.18	0.10-0.27	9 (47.36%)
		0.30-0.90	6(31.57%)
		1.2-2.5	3 (15.78%)
		8.6-10.10	1 (5.26%)
Indirect bilirubin mg/dl	0.27-0.82	0.29-0.80	10 (52.63%)
		1.0-1.20	6(31.57 %)
		2.45-8	3 (15.78%)
AST: aspartate aminotransferase; ALT: alanine aminotransferase; AF: alkaline phosphatase; TB: Total bilirubin; DB: direct bilirubin; IB: indirect bilirubin.			

TABLE IV: Thyroid profile in patients diagnosed with TC on ER admission from years 2007-2017 at INCMNSZ.

	Reference ranges	Average (quartiles) N = 19
TSH	0.34-5.60 uUI/ml	0.03 (0.02-0.04)
TT4	78.3-157 nmol/L	354.97 (243-718)
TT3	1.34-2.73 nmol/L	4.87(3.17-9.49)
T3 uptake	0.32-0.48	0.51 (0.46-0.56)
Thyroglobulin	0-30 ng/ml	113.54 (7.4-388)
Index TT3/TT4	>20 ng/ml	133 (2.63 -1573)
Index TL	30-115 nmol/l	166.4 (112.3-257.4)

Discussion

TC is a unique endocrine emergency, clinical evaluation should be the basis for suspecting and diagnosing TC, timely treatment will prevent permanent damage or death. In our study, the most relevant clinical data were tachycardia and fever. Graves' disease was confirmed in 57.2 percent of patients, with important physical signs including graves orbitopathy and goiter.

Thyroid storm is a rare emergency; However, in our Institute we have found 19 cases in the last 10 years, approximately 2 cases per year.

In Japan, in a study published by Akamizu Takashi et al. [4], they reported that TC was present in 77% of the women, the average age was 42 years old and the thyroid pathology identified in most cases was Graves' disease 95.2 % of the cases. In our study, 42.1% had poor adherence to taking their anti-thyroid drugs. 31.6% of the cases identified pneumonia as the triggering factor, followed by urinary tract infections and gastroenteritis in 10.5%. Only one patient developed TC following radioactive iodine therapy.

Methimazole induced agranulocytosis was reported only in 3 patients during their hospitalization, agranulocytosis subsided following thionamide discontinuation.

The AJT indicates within its criteria as a prerequisite, to obtain high free thyroid hormones samples; however, our patients only had total hormones determination, so if we are strict with this classification, our cases would correspond to a diagnosis of suspected TC. The clinical variables indicated by these Japanese criteria were present in all our patients in different combinations, so that the predominant symptom, which was present in 100% of the cases, was tachycardia, defined as a heart rate more than 130 beats per minute. Next, fever was reported in 13 of 19 patients (68.4%), defined as a temperature greater than 38 ° C; 57.9% of the patients had central nervous system abnormalities, defined by a Glasgow lower than 14 points. Gastrointestinal symptoms such as nausea, vomiting and diarrhea were described in 52.6% of the cases, it should be noted that within this group 5 patient had total bilirubin levels above 3mg / dl. Cardiovascular conditions reported included data of heart failure, characterized by the presence of scattered rales in more than 2/3 of the lung fields in 36.8% of patients. Of note some of them presented dyspnea and tricuspid valve failure, identified in 2 patients by echocardiography. Akamizu Takashi et al [4], reported tachycardia in 67.9%; 55.7% of the patients had a fever > 38 ° C; 64.2% had central nervous system involvement, 51.9% had gastrointestinal involvement and liver disorders. Heart failure it was present in 38.7%, data similar the clinical findings described in our study.

Furthermore, in our work we describe the biochemical characteristics in the patients admitted with TC diagnosis. Regarding renal function and electrolytes, 21.05% of the patients had BUN below normal ranges, as well as creatinine values, which were low in 78.94%. As reported by Iglesias et al [7], Hyperthyroidism is linked to a reduction in creatine

levels, due to the fact that thyroid hormones increase the activity of many co-transport systems in the renal tubule, including the Na-P co-transporter, the Na- exchanger. H and Na / K ATPase in the proximal convoluted tubule, resulting in an increased renal blood flow and GFR (glomerular filtration rate). Activation of the renin-angiotensin system and decreased resistance of the afferent glomerular arterioles lead to an increase in glomerular hydrostatic pressure and glomerular filtration. The increase in GFR and the reduction in total muscle mass cause a reduction in serum creatinine levels. The normalization of thyroid function can lead to normalization of kidney function, as occurred in all of our cases. Magnesium homeostasis abnormalities have been linked to hyperthyroidism; its clinical relevance is not yet fully understood. Thyroid hormones affect renal excretion and cellular transport of many electrolytes including magnesium, sodium and potassium [8].

Thyrotoxicosis is associated with a variety of liver function abnormalities. The pathogenesis of liver dysfunction has been attributed to mitochondrial dysfunction and hypoxia of liver tissue (9). In our study, 36.8% of the patients had elevated AST and ALT levels. In addition, 18 of 19 patients (94.7%) reported elevated alkaline phosphatase. Five patients presented total bilirubin levels above 3mg / dl, only one patient had a level 12mg / dl, mainly driven by direct bilirubin.

The clinical criteria defined by the Japanese society, 100% of our patients had a heart rate greater than 130 beats per minute followed by fever that occurred in 68% of the patients. The mortality rate in this group of patients is higher. The main culprit likely mainly related to multi-organ failure and another substantial proportion by heart failure. By receiving immediate treatment, it is possible that progression to these fatal outcomes could had been prevented.

Almost all patient who were part of this study received standard of care treatment for TC, we only lost track of one patient who requested medical discharge and did not attend subsequent check-ups, the rest of the patients had his definitive treatment, 52.6% were treated with radioactive Iodine therapy, 26.3 % underwent total thyroidectomy. Currently, these patients continue to attend their follow up visit at our continuity of care thyroid clinic.

Bibliographic References

1. De Leo S, Sun Y Lee, and Lewis E Braverman. Hyperthyroidism. *Lancet*. 2016.
2. Alzamani Mohammad Idrose. Acute and emergency care for thyrotoxicosis and thyroid storm. *Acute Medicine Surgery*, 2015.
3. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, Rivkees SA, Samuels M, Sosa JA, Stan MN, Walter MA. American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. *Thyroid Journal*, 2016

4. Takashi Akamizu, Tetsurou Satoh, Osamu Isozaki, Atsushi Suzuki, Shu Wakino, Tadao Iburi, et al. Diagnostic Criteria, Clinical Features, and Incidence of Thyroid Storm Based on Nationwide Surveys. *Thyroid Journal*. 2012
5. Alzamani Mohammad Idrose. Acute and emergency care for thyrotoxicosis and thyroid storm. *Acute Medicine Surgery*, 2015.
6. Iglesias P, Bajo M, Selgas R y Díez J. Thyroid dysfunction and kidney disease: An update. *Reviews in Endocrine and Metabolic Disorders*, 2017.
7. Tumba Disashi, Taisuke Iwaoka, Junnosuke Inoue, Shojiro Naomi, Yasuko Fujimoto, Teruhisa umed, et al. *Endocrine Journal* 1996.
8. Tariq Mehmood Khan, Saqib Malik, Inayat Ullah Diju. Correlation between plasma thyroid hormones and liver enzymes level in thyrotoxic cases and controls in hazara division. *Journal of Ayub Medical College Abbottabad*, 2010.
9. Malik R and Hodgson H. The relationship between the thyroid gland and the liver. *QJM: An International Journal of Medicine/Oxford Academic*, 2002.