

Thyroid Storm Presenting as Jaundice and Complete Heart Block

S C Ho,**MBBS, M Med, MRCP (UK)*, P H K Eng,**MBBS, MRCP (UK)*, Z P Ding,***FAMS, MBBS, M Med*,
A C K Fok,****FAMS, MRCP (UK), M Med*, D H C Khoo,*****FAMS, MRCP (UK), M Med*

Abstract

Thyroid storm is a difficult diagnosis in “apathetic” variant of hyperthyroidism. The clinical features may not be evident. Abnormal atrioventricular (AV) conduction, such as complete heart block, in thyrotoxicosis is uncommon. We report a case of a 16-year-old girl presenting with fever, jaundice, heart failure and complete heart block in whom the diagnosis of thyroid storm was initially missed because of the unusual presenting features. Prompt resolution of the conduction abnormality occurred when treatment with carbimazole, intravenous iodide and dexamethasone was instituted.

Ann Acad Med Singapore 1998; 27:748-51

Key words: Atrio-ventricular conduction, Heart failure, Mitral valve prolapse, Thyrotoxicosis

Introduction

Thyroid storm is defined as a severe and often life-threatening exacerbation of thyrotoxicosis which is usually characterised by hyperthermia, tachycardia, severe agitation and altered mental status.¹⁻³ With the “apathetic” variant of hyperthyroidism, the classical features may not be evident. Thyroid storm is even more difficult to diagnose in patients with an unusual presentation such as status epilepticus, cerebral infarction or acute renal failure.⁴ The diagnosis of thyroid storm is usually not considered in the absence of tachycardia.¹⁻³ Hyperthyroidism is commonly associated with sinus tachycardia and cardiac arrhythmias, particularly atrial fibrillation. However, atrioventricular conduction abnormalities in this disorder have been well documented.⁵⁻¹⁶ We report a case of a 16-year-old girl presenting with fever, jaundice and complete heart block in whom the diagnosis of thyroid storm was initially missed because of the unusual presenting features.

Case Report

A 16-year-old Chinese girl from a neighbouring country was admitted with a 4-week history of fever, chills and rigors. This was associated with right hypochondrial pain, passage of tea-coloured urine, diarrhoea, vomiting and recurrent episodes of syncope.

The patient had been diagnosed to have Graves' dis-

ease 5 years ago and treated with multiple courses of carbimazole. This was her 4th relapse and she was restarted on carbimazole and scheduled for subtotal thyroidectomy. She had a history of childhood asthma and was allergic to propylthiouracil. There was no past history of rheumatic fever or any cardiac abnormality.

Soon after the relapse, the patient developed diarrhoea and vomiting for 2 weeks and was treated for gastroenteritis. This was followed by giddiness and 3 brief episodes of syncope. She also became progressively jaundiced and complained of right hypochondrial pain. She was admitted and observed to have occasional episodes of bradycardia with no documentation of conduction abnormalities. A diagnosis of congestive heart failure was made and she was prescribed carbimazole 10 mg tid, frusemide 40 mg om, KCl 0.6 g om and digoxin 0.0625 mg om. When she had not improved after 5 days, she was transferred to our centre.

Physical examination revealed a thin and lethargic young girl weighing only 35 kg. She was pale, jaundiced and febrile with a temperature of 38.5°C. Her blood pressure and pulse rate were 110/50 mmHg and 70/min respectively. Her apex beat was heaving and displaced and there was a pan-systolic murmur at the left sternal edge radiating to the axilla. Clinically, she was in heart failure with elevated jugular venous pressure, pedal oedema and bilateral basal lung crepitations. The liver

* Registrar

*** Senior Consultant and Head

**** Consultant and Director of Thyroid Unit

Department of Endocrinology

Singapore General Hospital

** Consultant

Singapore Heart Centre

Address for Reprints: Dr Ho Su Chin, Department of Endocrinology, Singapore General Hospital, 1 Hospital Drive, Singapore 169608.

was enlarged and tender. A smooth diffuse goitre was palpable but there were no tremors or diaphoresis. She appeared euthyroid and apathetic. The initial clinical diagnoses were acute hepatitis and heart failure due to Graves' disease.

Chest X-ray showed cardiomegaly and a right pleural effusion. Electrocardiography (ECG) showed complete heart block, p mitrale and left ventricular hypertrophy (Fig. 1). A temporary transvenous cardiac pacing wire was inserted. Stool, urine and blood cultures were taken. Table I shows the trend of blood investigation results performed. In view of the clinical and ECG findings, a diagnosis of infective endocarditis was considered. The patient was continued on her previous medications and intravenous antibiotics were added.

Transthoracic two-dimensional echocardiography showed mitral and tricuspid valve prolapse with moderate mitral and tricuspid regurgitation. No vegetation

was found. The left ventricle was dilated with hyperdynamic systolic function and ventricular ejection fraction was estimated at 77%. There was moderate left atrial and mild right atrial dilatation with pulmonary hypertension. A transeosophageal echocardiography also did not detect any valvular vegetation. Investigations did not localize any infection. Blood, urine and stool cultures were sterile. Ultrasound of the abdomen showed an enlarged liver with no other abnormal findings. Screens for hepatitis A, B and C were negative. Autoimmune markers such as anti-nuclear antibody and anti-double-stranded DNA antibody were negative.

When her condition did not improve over the next 24 hours, she was treated for thyroid storm with carbimazole 15 mg tid, intravenous dexamethasone 4 mg 8 hourly and intravenous sodium iodide 1 g 12 hourly for 2 days. There was dramatic improvement with this treatment. By the next day, the patient was afebrile and the diar-

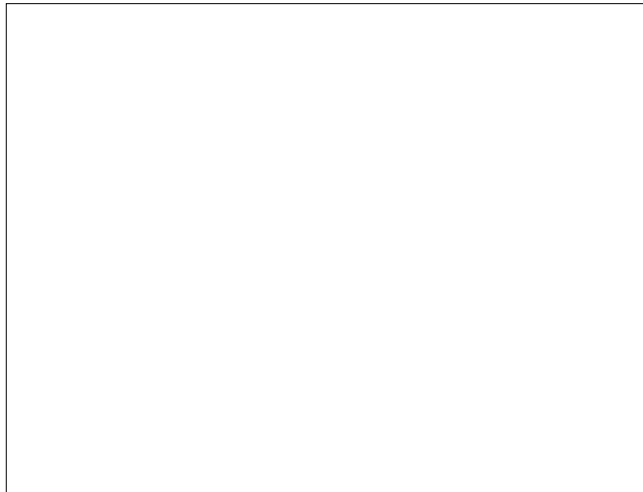


Fig. 1. Electrocardiogram showing complete heart block on the day of admission.

TABLE I: RESULTS OF BLOOD INVESTIGATIONS DONE DURING PATIENT'S ADMISSION

Parameter	Normal range	Before treatment	After treatment*
Total white cell count (x 10 ⁹ /L)	4.0 - 10.0	14.6	5.2
Neutrophils (%)	40 - 75	77.4	80.5
Erythrocyte sedimentation rate (mm/hour)	3 - 15	63	45
C-reactive protein (mg/L)	1 - 10	33	1
Total protein (g/L)	62 - 82	64	70
Albumin (g/L)	37 - 51	23	25
Bilirubin (µmol/L)	3 - 24	77	56
Alkaline phosphatase (U/L)	119 - 351	103	106
Alanine transaminase (U/L)	7 - 36	33	16
Aspartate transaminase (U/L)	15 - 33	21	22

* Results obtained about 1 week after starting definitive treatment

TABLE II: TREND OF THYROID FUNCTION TESTS DURING THE COURSE OF PATIENT'S ILLNESS

Parameter	Normal range	In-patient		Out-patient	
		Before treatment	After treatment*	1 month post-RAI	5 months post-RAI
Free T ₄ (pmol/L)	10.3 - 31.0	50.5	20.1	11.9	16.0
TSH (mU/L)	0.52 - 5.04	0	0	0	0.12
Total T ₃ (nmol/L)	1.2 - 3.4	-	0.9	-	-
TRAB (U/L)	<10	64.4	-	-	191.3
TgAB (U/L)	0 - 0.3	34.6	-	-	-
TPOAB (U/L)	0 - 0.3	33.1	-	-	-

Free T₄ : free thyroxine RAI : radioactive iodine

TSH : thyroid stimulating hormone

TRAB : TSH receptor antibody

TgAB : anti-thyroglobulin antibody

TPOAB : anti-thyroperoxidase antibody

* Results obtained about 1 week after starting definitive treatment

rhoea had stopped. Table II shows the trend of the thyroid function tests during admission and on follow up. The AV block had improved to a second degree Mobitz type 1 heart block on the 3rd day and a first-degree heart block on the 6th day. The patient was eventually treated with 15 mCi of radioactive iodine 131.

One month after radioiodine, ECG showed a normal PR interval. She had gained 6 kg of weight. Two-dimensional echocardiography repeated after 5 months showed mitral valve prolapse with moderate mitral regurgitation. The tricuspid regurgitation was trivial. Left atrial, right atrial and left ventricular sizes were normal and the left ventricular ejection fraction was estimated at 55%. An ECG done at this time showed resolution of the p mitrale and left ventricular hypertrophy.

Discussion

Thyroid storm has been defined as a life-threatening exacerbation of thyrotoxicosis. The diagnosis is essentially a clinical one since there is no differentiation between the two based on circulating thyroid hormone levels.⁴ There are no standard criteria for the diagnosis of thyroid storm although it is widely accepted that the cardinal features include tachycardia, fever, agitation and an abnormal mental state.¹⁻³ Dysfunctions of the cardiovascular and gastrointestinal systems are often present.^{2,3} In thyrotoxicosis, the predominant cardiac complications are atrial tachyarrhythmias and heart failure. Atrial fibrillation is the most common, occurring in 10% to 22% of hyperthyroid patients.¹⁷ Although the tachyarrhythmias of hyperthyroidism have been well documented, AV conduction abnormalities in thyrotoxicosis were seldom reported. Stern et al⁵ reported first degree heart block in 2% to 30% of cases while second and third degree heart blocks were very rare. A review of the literature revealed less than 20 cases of complete heart block associated with hyperthyroidism.⁵⁻¹⁶

Because of a lack of awareness of the above association, the physicians involved in the initial management had underestimated the severity of her hyperthyroidism. Burch and Wartofsky⁴ had proposed a diagnostic point scale for thyroid storm in which a score of 45 was highly suggestive of thyroid storm. Our patient scored 75 points on this scale. She had presented with an acute febrile illness resembling a hepatobiliary infection. Hepatitis markers were negative and antibiotic treatment did not give prompt improvement. Septic work-up and ultrasound imaging did not identify an infective cause. Gastrointestinal symptoms such as diarrhoea, vomiting and jaundice featured prominently in this case. Jaundice occurs in thyrotoxicosis as a result of liver congestion from heart failure or from hepatocellular dysfunction. It is present in up to 20% of patients with thyroid storm.¹⁸ The clinical picture, the high free T4 coupled with the rapid response to iodide and steroid therapy in this

patient confirmed the diagnosis of thyroid storm.

The factors that might have contributed to the development of complete heart block in this case include prior digoxin administration and the presence of valvular heart diseases. However, digoxin had been used at a low dose and for a short duration of 5 days. The serum digoxin level was also sub-therapeutic suggesting that digoxin probably did not contribute significantly to the development of complete heart block. Moreover, bradycardia had been noted before digoxin usage although this had not been documented on ECG. The cause of the AV conduction abnormalities in Graves' disease is unknown. While cardiac abnormalities such as mitral stenosis¹² and mitral regurgitation^{14,15} had been described as possible aggravating factors, the authors had not explained the pathogenesis of AV dissociation in hyperthyroidism. The complete normalization of PR interval in our patient after euthyroidism suggested that her valvular heart disease was not associated with primary conduction anomalies. In the majority of hyperthyroid cases with complete heart block, there were preceding histories of acute infections.^{5,8,12} In one such case, post-mortem examination revealed infiltration of the AV node and bundle of His by polymorphs and gram-positive cocci.¹² In addition to co-existing cardiac anomalies^{12,14} and digoxin,¹² other contributing factors included hypokalaemia,^{11,16} hypercalcaemia¹⁹ and drugs other than digoxin.^{9,14} However, in some cases, no cause had been identified and thyrotoxicosis was the sole reason of the conduction abnormality.¹³ Autopsies in patients with fatal hyperthyroidism showed dilated ventricles, myocyte hypertrophy, "myocardial oedema", interstitial and perivascular fibrosis, cellular infiltration and myocyte necrosis.²⁰ Reversible myocardial damage due to hyperthyroidism demonstrated by In¹¹¹-labelled monoclonal antimyosin antibodies had been reported.²¹ Although the heart block in our patient could have been a result of a focal myocarditis affecting the region around the AV node,¹⁶ the rapid response to therapy suggested a metabolic aetiology rather than myocardial necrosis. Thyroid hormones are known to have a direct effect on the intrinsic sinoatrial electrophysiologic function. While thyroid hormones usually decrease conduction time, it appears that in certain patients nodal blocks may result instead.²² Miller et al¹⁰ had demonstrated AV nodal block utilizing a His bundle ECG in a Graves' disease patient with second and third degree AV block.¹⁰ They had commented that heart block appears to occur in those patients with severe or long-standing disease.

Conclusion

The pathophysiology of AV conduction abnormalities in thyrotoxicosis is not well understood. Nonetheless, there had been well-documented cases in which these conduction abnormalities had resolved rapidly with

treatment of the thyrotoxicosis. In at least 2 cases His bundle ECG had demonstrated AV nodal blocks. The patients at risk appear to be those with long-standing or severe disease. Failure to recognize heart-block due to thyrotoxicosis may result in unnecessary morbidity and mortality. We have reported a case of thyroid storm which initially went unrecognized because of the unusual presenting features of jaundice and complete heart-block and described the rapid ECG changes which occurred once treatment for thyroid storm was initiated.

REFERENCES

1. Rives J D, Shepard R M. Thyroid crisis. *Am Surg* 1951; 17:406-18.
2. Waldstein S S, Slodki S L, Kaganiec G I, Bronsky D. A clinical study of thyroid storm. *Ann Intern Med* 1960; 52:626-42.
3. Mazzaferri E L, Skillman T G. Thyroid storm: A review of 22 episodes with special emphasis on the use of guanethidine. *Arch Intern Med* 1969; 124:684-90.
4. Burch H B, Wartofsky L. Life-threatening thyrotoxicosis: Thyroid storm. *Endocrinol Metab Clin North Am* 1993; 22:2:263-78.
5. Stern M P, Jacobs R L, Duncan G W. Complete heart block complicating hyperthyroidism. *JAMA* 1970; 212:2117-9.
6. Hoffman I, Lowrey R D. The electrocardiogram in thyrotoxicosis. *Am J Cardiol* 1960; 6:893-904.
7. Blizzard J J, Rupp J J. Prolongation of the PR interval as a manifestation of thyrotoxicosis. *JAMA* 1985; 173:1845.
8. Kernoff L M, Rossouw J E, Kennelly B M. Complete heart block complicating thyrotoxicosis. *SAfr Med J* 1973; 47:513-5.
9. Kramer M R, Shilo S, Hershko C. Atrioventricular and sinoatrial block in thyrotoxic crisis. *Br Heart J* 1985; 54:600-2.
10. Miller R H, Corcoran F H, Baker W P. Second and third degree atrioventricular block with Graves' disease: a case report and review of the literature. *Pacing Clin Electrophysiol* 1980; 3:702-9.
11. Ee B, Cheah J S. Electrocardiographic changes in thyrotoxic periodic paralysis. *J Electrocardiol* 1979; 12:263-70.
12. Davis C A, Smith H L. Complete heart block in hyperthyroidism following acute infections: A report of 6 cases with necropsy finding in 1 case. *Am Heart J* 1933; 9:81-9.
13. Steuer L G. Complete heart block in hyperthyroidism. *Am Heart J* 1936; 11:623-5.
14. Muggia A L, Stjernholm M, Houle T. Complete heart block with thyrotoxic myocarditis. *N Engl Med J* 1970; 283:1099-100.
15. Eraker S A, Wickamasekaran R, Goldman S. Complete heart block with hyperthyroidism. *JAMA* 1978; 239:1644-6.
16. Yusoff K, Khalid B A K. Conduction abnormalities in thyrotoxicosis—a report of three cases. *Ann Acad Med Singapore* 1993; 22:609-12.
17. Ladenson P W. Recognition and management of cardiovascular disease related to thyroid dysfunction. *Am J Med* 1990; 88:638-41.
18. Sherlock S. *Disease of the Liver and Biliary System*. 4th ed. Oxford: Blackwell Science, 1968:512.
19. Sataline L, Donaghue G. Hypercalcemia, heart block and hyperthyroidism. *J Am Med Assoc* 1970; 213:1342.
20. Shirani J, Barron M M, Pierre-Louis M L, Roberts W C. Congestive heart failure, dilated cardiac ventricles, and sudden death in hyperthyroidism. *Am J Cardiol* 1993; 72:365-8.
21. Marti V, Ballester M, Obrador D, Moya C, Carrio I, Pons-Llado G. Active myocardial damage in hyperthyroidism: a concurrent mechanism of heart failure reversed by treatment. *Eur Heart J* 1995; 16:1014-6.
22. Valcavi R, Menozzi C, Roti E, Zini M, Lolli G, Roti S, et al. Sinus node function in hyperthyroid patients. *J Clin Endocrinol Metab* 1992; 75:239-42.