

Original papers

QJM

Thyrotoxicosis and acute abdomen—still as defying and misunderstood today? Brief observations over the recent decade

M.K.-S. LEOW, D.E.-K. CHEW, M. ZHU and P.-C. SOON

From the Department of Endocrinology, Division of Medicine, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433

Received 20 October 2007 and in revised form 16 August 2008

Summary

Background: Clinicians managing thyrotoxic patients with acute abdomen face challenging diagnostic and risky therapeutic dilemmas.

Aim: To analyse the frequency of medical vs. surgical acute abdomen, and to characterize the poorly understood thyrotoxic medical acute abdomen phenomenon.

Design: Retrospective review of case notes.

Methods: All case files with a simultaneous diagnosis of thyrotoxicosis and acute abdomen admitted between 1994 and 2004 were traced and audited.

Results: Thirteen had a history of thyrotoxicosis while 12 were newly diagnosed. The commonest cause was Graves' disease. Twenty-three (92%) cases were thyrotoxic, of whom six (24%) had thyroid crisis, while two (8%) had subclinical

thyrotoxicosis. The provisional diagnosis of acute abdomen was correct in 14 cases (56%), but discordant with the final diagnosis in 11 cases (44%). Eight cases (32%) without any demonstrable pathology were medical, vs. four (16%) with surgical acute abdomen, while 11(44%) had gastritis, hepatobiliary–pancreatic disorders or diverticulitis conservatively managed. The epigastrium and/or central abdomen (72.7%) were the commonest affected regions in medical acute abdomen.

Conclusions: Although the majority of acute abdomen in thyrotoxicosis was medical in nature, our experience indicates that surgical conditions were not uncommon. Thus, serious causes requiring life-saving surgery should be excluded before attributing it to medical acute abdomen.

Introduction

The acute abdomen is defined as severe abdominal pain with rebound tenderness and abdominal guarding. Usually, the causes are due to surgical conditions necessitating prompt surgical intervention. However, there are certain mimicking 'medical conditions' typified by absence of true surgical

disorders. These include uncontrolled thyrotoxicosis/thyroid crisis, Addisonian crisis, diabetic ketoacidosis, pheochromocytoma crisis, tabetic crisis, hereditary angioedema, lead poisoning and acute porphyria. Among these, thyrotoxicosis is one of the commonest causes of the 'medical acute

Address correspondence to M.K.-S. Leow, Department of Endocrinology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433. email: mleowsj@massmed.org

abdomen'.¹ Although enshrouded in mystery,² various pathogenetic mechanisms have been proposed, including thyrotoxicosis-induced hypermotility with mechanical stretch triggering visceral nociception,^{3,4} and mesenteric ischaemia from sympathetic supersensitivity⁵ with resultant release of pro-inflammatory pain-mediating cytokines acting on gut mucosal receptors.⁶ Undoubtedly, differentiating medical from surgical aetiologies to balance the benefit of emergency operations against the risk of precipitating thyroid crisis is crucial, yet disputes between physicians and surgeons regarding the contributory role of thyrotoxicosis in acute abdomen may delay life-saving surgery. This audit was carried out with such considerations in mind and represented a revisit to one of medicine's well-established dilemmas.

Objectives

Our retrospective analysis audited all patients with thyrotoxicosis and concomitant acute abdomen between 1994 and 2004. The objectives included an evaluation of the frequency of true medical acute abdomen related to thyrotoxicosis and to characterize this obscure phenomenon.

Methods and subjects

Using International Classification of Diseases, 9th revision (ICD-9) classification codes, all case files of patients admitted between 1994 and 2004 in Tan Tock Seng Hospital with a simultaneous diagnosis of thyrotoxicosis (or hyperthyroidism) and acute abdomen were identified from the hospital database. Twenty-five patients who fitted this category were found and analysed. Being a retrospective audit done as part of an institutional effort to improve clinical care without evaluating research hypotheses, it was exempted from ethical review. The baseline demographic characteristics are shown in Table 1.

Table 1 Demographic Characteristics of Sample Population

Demographic	Value
Age (years)	51.2 ± 14.4 (29.3–88.0)
Gender ratio	15 (females) : 10 (males)
Ethnic distribution	Chinese (20) : Malay (3) : others (2)
Etiology of hyperthyroidism	Graves' disease (21) : toxic MNG (1)
Discipline admitted	Surgical (13) : medical (12)

Results

Audit of clinical features

Thirteen had a history of thyrotoxicosis while 12 were newly diagnosed. A goitre was discernible in 21 patients while absent in 4. The epigastrium is frequently affected in those with medical acute abdomen (Table 2).

Among the 13 with underlying thyrotoxicosis, 4 were on Antithyroid Drug (ATD) therapy for over 2 years, 5 for <2 years and 4 were treated over an undetermined period due to poor compliance with ATD. Twenty-three cases were biochemically thyrotoxic with at least one of the classical symptom of heat intolerance, weight loss, palpitations, tremors, hyperhidrosis or hyperphagia, except for two patients who were totally asymptomatic despite being biochemically toxic [Patient 1: free thyroxine (T4) 81 pmol/l, Thyroid Stimulating Hormone (TSH) <0.005 mIU/l; Patient 2: free T4 74 pmol/l, TSH <0.005 mIU/l]. Both were above the age of 50 years and therefore had apathetic thyrotoxicosis. Two (8%) had subclinical thyrotoxicosis.

Audit of laboratory and radiological tests ordered

Free T4 and TSH were performed in every case with a positive history, thyrotoxic features and whenever medical acute abdomen was suspected. Free T4 was assayed using chemiluminescence immunoassay (ACS-180-Plus analyzer, CIBA Corning Diagnostic Corp., Medfield, MA, USA) and TSH via third-generation Immunochemiluminometric Assay (ICMA) (Access TSH Assay, Sanofi Diagnostics Pasteur, Inc., Chaska, MN, USA). TSH receptor autoantibody

Table 2 Outcomes of Selected Audit Variables

Outcome	Value <i>n</i> (%)
Demonstrable pathology by radiography or endoscopy	11 cases (44)
Surgical abdomen	4 cases (16)
Medical abdomen	8 cases (32)
Most frequently affected region in medical acute abdomen	Epigastrium and/or central abdomen (72.7)
Met criteria of thyroid crisis	6 cases (3 medical: 3 surgical)
Provisional diagnosis of acute diagnosis compared with final diagnosis	Concordant 14 cases (56)
	Discordant 11 cases (44)

was assayed by human recombinant TBII assay (DYNOfest® TRAK human, BRAHMS AG, Berlin, Germany). The distribution of free T4 values among all 25 patients is shown in Figure 1.

As polymorphonuclear leucocytosis is present in most cases of true surgical abdomen, we examined if this helped to discriminate medical from surgical abdomen. The overwhelming majority [seven of eight (87.5%) patients] with medical acute abdomen had a total white cell count of $<12\,000/\mu\text{l}$ (range 6500–11 400; mean 8870), associated with normal differential leucocyte counts in four patients. Three had normal leucocyte count associated with mild neutrophilia. Only one patient had a pronounced leucocytosis of $29\,200/\mu\text{l}$ (90.2% neutrophils) eventually attributed to infective gastroenteritis. Approximately 50% (8 of 17 patients) of those with surgical abdomen had leucocytosis exceeding $12\,000/\mu\text{l}$ (range 5000–22 600; mean 12 200), all of whom also had neutrophilia (i.e. $>75\%$ neutrophils on differential counts). Neutrophilia was also present in two of the remaining nine with leucocyte count $<12\,000/\mu\text{l}$.

The most frequently ordered imaging test was a plain abdominal radiograph (24 of 25 patients), followed by abdominal ultrasonography (12 of 25 patients) and abdominal CT scan (6 of 25 patients).

Audit of accuracy of preliminary diagnosis and correlation with final diagnosis

Figures 2 and 3 provide an overall summary of how the initial preliminary clinical diagnosis compared with the final diagnosis of the acute abdomen.

None of those with a final diagnosis of medical acute abdomen had abdominal surgery, though flexible oesophagogastroduodenoscopy was used to evaluate two of them. In contrast, six patients with surgical acute abdomen underwent major surgery.

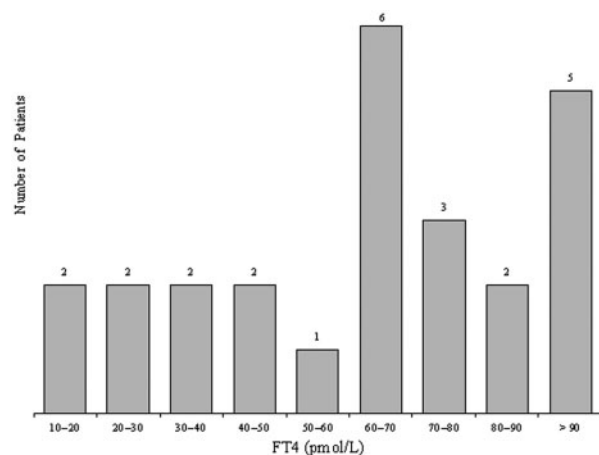


Figure 1. Distribution of FT4 values on admission.

Three had appendectomy, two had laparotomy and one had laparoscopic cholecystectomy. Another patient had endoscopic retrograde cholangiopancreatography, but did not undergo major surgery.

Audit of comorbidities, complications and adverse events

Using Burch and Wartofsky's criteria,⁷ six patients had thyroid crisis. Although it is known that thyroid crisis may occur even in patients with only modestly elevated serum-free T4 levels,² their serum-free T4 exceeded 50 pmol/l (range 65 to >90 pmol/l). Two were poorly compliant with ATD treatment, two were newly diagnosed and were on ATD for

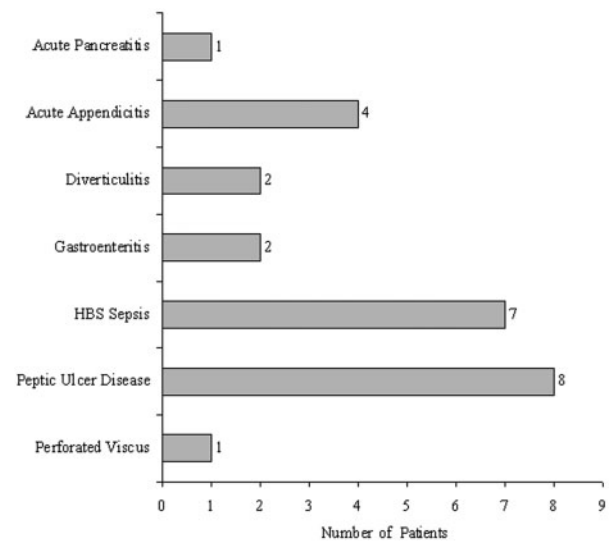


Figure 2. Initial preliminary clinical diagnosis of acute abdomen.

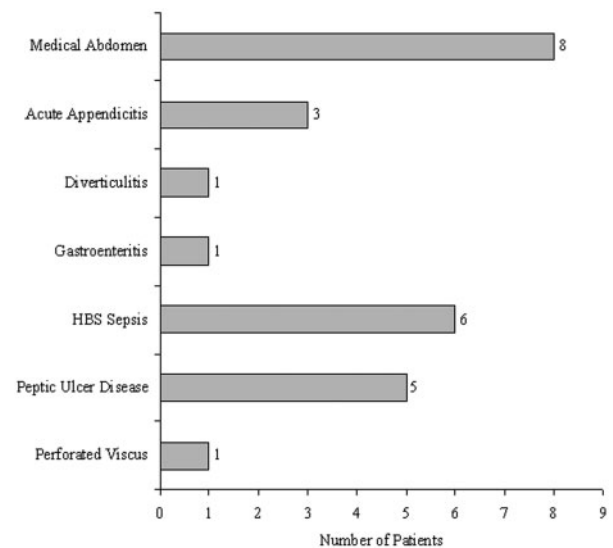


Figure 3. Final confirmed diagnosis of acute abdomen.

between 1 and 3 months, and two were on ATD treatment for over a year. Among them was a 46-year-old Malay female with newly diagnosed Graves' disease who suffered a cardiac arrest and died. This was the only mortality recorded. Another 48-year-old Chinese woman with rapid atrial fibrillation and underlying hyperthyroidism suffered a cardiovascular collapse shortly following oral propranolol (20 mg tds) administration and was successfully resuscitated. She was normokalaemic but had mild hypomagnesaemia of 0.67 mmol/l. All six patients with thyroid storm were offered I-131 thyroid ablation, yet only two underwent I-131 therapy while four refused.

As comorbidities can influence the perioperative risks of exploratory laparotomy in acute abdomen, we also examined how many patients had at least one other chronic illness. Only eight patients had no medical problems pre-morbidly. But 17 patients had some form of pre-existing medical problem. Of these, four patients had type 2 diabetes mellitus, four had hypertension, two had stroke, one had thyrocardiac disease and one had ischaemic heart disease and two has bronchial asthma. Another three patients had other conditions (pernicious anaemia, HBV carrier and psoriasis).

Discussion

This is an audit on patients with a simultaneous diagnosis of acute abdomen and thyrotoxicosis. Only 25 such patients were encountered in our institution over a span of a decade, likely reflecting that the occurrence of this combination of two problems is either uncommon or possibly under-recognized. An obvious limitation with this audit is the reliance on a computerized search of the database via diagnosis-related groups, since omissions or errors in coding could contribute to under-tracing. Nevertheless, this audit has yielded some interesting insights and provocative findings.

First, Graves' disease formed the majority and a goitre was consistently present. Nearly a quarter was complicated by thyroid crisis at the time of presentation of the acute abdomen. As thyroid crisis itself constitutes a grave emergency posing major perioperative risks, its stabilization is often a medical priority that may delay life-saving surgery.⁸ The corollary is equally true, that patients with medical or surgical acute abdomen who undergo emergency surgery without having their thyrotoxicosis stabilized adequately or whose newly developed thyrotoxicosis was missed can degenerate into thyroid storm during or after surgery.⁹ The diagnosis of thyrotoxicosis is straightforward when classical

signs and symptoms are present. Our audit revealed two cases (excluding subclinical thyrotoxicosis) with apathetic thyrotoxicosis. It is therefore crucial that patients are not sent for surgery until thyrotoxicosis has been evaluated to minimize perioperative morbidity and mortality.

Second, additional testing that may assist in diagnosing a true surgical abdomen is an ideal but tricky and elusive goal. We found imaging to be helpful. However, though the plain abdominal radiograph is often performed, urgent ultrasound and abdominal CT proved to have higher sensitivities in detecting surgical conditions and were often the factor that influenced the clinical decision-making process. We also recognized that many cases of medical acute abdomen had normal total white cell and differential counts while half of all surgical abdomens had polymorphonuclear leucocytosis.

A major objective is to unravel the accuracy of a medical or surgical acute abdomen diagnosed clinically. The high discordant rate of 44% between the provisional with the final diagnosis is consistent with an epidemiological study of acute abdominal pain concluding that the overall sensitivity of history taking and physical examination in making a diagnosis was poor.¹⁰ Hence, further investigations including blood leucocyte counts, C-reactive protein and abdominal imaging are required to improve the diagnostic accuracy.

An important implication is that a medical acute abdomen misdiagnosed as a surgical acute abdomen would potentially lead to needless major surgery. This not only exposes the patient to the risks of unnecessary surgery, but also subjects such patients to the hazard of potential thyroid crisis. We showed that the diagnosis of medical acute abdomen was largely made after having excluded major surgical conditions. As such, all those finally confirmed to have medical acute abdomen were not operated upon. Arguably, this outcome was purely fortuitous and the risk of diagnosing surgical acute abdomen wrongly leading to unnecessary surgery remains difficult to avoid in reality. Conversely, misdiagnosing a surgical for a medical acute abdomen is also a grave error, since the consequences can be catastrophic and possibly fatal. Many doctors are aware of the pitfalls and dangers of assuming acute abdomen in thyrotoxic patients to be medical in nature, since all those cases reclassified as medical acute abdomen was initially considered to be surgical. This underscores the importance of thorough physical examination combining pertinent investigations that aid diagnosis. Finally, five of eight patients with medical acute abdomen were treated with propranolol, raising the

possibility of iatrogenic mesenteric ischaemia from β -adrenergic blockade-induced splanchnic vasoconstriction. As long-acting β -blockers are frequently used in thyroid crisis,¹¹ this is an area worthy of future investigation. Concurrent presentation of acute abdomen and thyrotoxicosis will continue to plague infirmaries ubiquitously and challenge the wits of many respectable clinicians. Given the dearth of studies on this area, our results might contribute some useful insights impacting positively on clinical practice.

Conclusions

Thyroid storm is a known cause of medical acute abdomen. Nevertheless, it behooves both physicians and surgeons to evaluate for potential surgical causes. Based on this audit, clinicians are recommended to exercise careful judgement, taking into account both laboratory and radiological data before deciding on a conservative or interventional approach.

Acknowledgements

The patient proofreading and secretarial assistance of Sim-Joo Tan and encouraging inputs of Eunice May-Jane Leow throughout the preparation of this manuscript are well appreciated.

Conflict of interest: None declared.

References

1. Steinheber FU. Medical conditions mimicking the acute surgical abdomen. *Med Clin North Am* 1973; **57**:1559–67.
2. Bhattacharyya A, Wiles PG. Thyrotoxic crisis presenting as acute abdomen. *J R Soc Med* 1997; **90**:681–2.
3. Ray BS, Neill CL. Abdominal visceral sensation in man. *Ann Surg* 1947; **126**:709–24.
4. Groskreutz JL, Kim CH, McConahey WM. Acute gastroparesis associated with thyrotoxicosis. *Am J Gastroenterol* 1990; **85**:1206–7.
5. Grassby PF, McNeill JH. Hyperthyroidism induces supersensitivity to biogenic amines in rat vascular tissue via a pre- and a postjunctional mechanism. *J Pharmacol Exp Ther* 1988; **244**:1027–35.
6. Cervero F. Neurophysiology of gastrointestinal pain. *Baillieres Clin Gastroenterol* 1988; **2**:183–99.
7. Burch HB, Wartofsky L. Life-threatening thyrotoxicosis: thyroid storm. *Endocrinol Metab Clin North Am* 1993; **22**:263–77.
8. Langley RW, Burch HB. Perioperative management of the thyrotoxic patient. *Endocrinol Metab Clin North Am* 2003; **32**:519–34.
9. Pronovost PH, Parris KH. Perioperative management of thyroid disease. Prevention of complications related to hyperthyroidism and hypothyroidism. *Postgrad Med* 1995; **98**:83–6, 96–8.
10. Yamamoto W, Kono H, Maekawa H, Fukui T. The relationship between abdominal pain regions and specific diseases: an epidemiologic approach to clinical practice. *J Epidemiol* 1997; **7**:27.
11. Koksas AS, Uskudar O, Koklu S, Yuksel O, Beyazit Y, Sahin B. Propranolol-exacerbated mesenteric ischemia in a patient with hyperthyroidism. *Ann Pharmacother* 2005; **39**:559–62.