

中文題目：甲狀腺亢進治療藥物導致白血球減少症：病例報告及文獻回顧

英文題目：Carbimazole Induced Leucopenia : Case Report and Review of Literature

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Introduction

Anti-thyroid drugs are commonly used to control hyperthyroidism, especially when patients refuse other therapies such as radioiodine and surgery. Idiosyncratic drug-induced agranulocytosis is a severe selective depression of myelopoiesis. Herein we reported a case of typical presentation of carbimazole induced leucopenia.

Case Presentation

A 33 years old man was presented with high fever 39.5°C since 1 day. He was diagnosed as thyrotoxicosis due to Graves' disease since last two months and regular Carbimazole 20 mg twice daily at our endocrinology department. He had no history of systemic illness before. Last two months ago, he visited to our endocrinology department due to body weight loss 3-4 kg within 1-2 months, he also felt palpitation for 2-3 days, easily anxiety occurred. He also mentioned heat intolerance but he did not mention no dry mouth and thirsty nor frequency of urine.

At emergency department, routine investigation including CBC/DC, renal function, electrolyte, CRP, chest X ray, urine routine was checked up. CBC, DC revealed neutropenia, leucopenia. Emergency medical officer prescribed him adequate hydration also give (G-CSF) granulocyte colony stimulating factors 2 vials and as well as empiric antibiotic immediately for prevent sepsis. After arrival to ordinary ward, his vital signs revealed body temperature 38.7°C, pulse rate was 103/min, respiratory rate was 19/min, blood pressure was 117/57mmHg.

On system review revealed headache when attack of fever but without convulsion or conscious change, no meningeal sign. On physical examination revealed general condition was well-being but acute ill looking. Eye show no pallor over conjunctiva, mild exophthalmos, neck

show huge goiter, supple, no lymphadenopathy, bruit on auscultation. Lung show clear breathing sound over bilateral lung field. Heart beat was rapid, regular. Abdomen show soft, bowel sound was normoactive, Extremities show hand tremor when hand was extended, no pitting edema.

After admitted to ward, we prescribed empirical antibiotic Ceftazidime 2-gram 8 hourly and Teicoplanin 600 mg 12 hourly, also gave adequate hydration to him. We stopped anti-thyroid agents Carbimazole and gave him propranolol 10 mg for control hand tremor as well as for tachycardia, also gave lithium 300 mg twice daily. After his general condition became improved, fever was subsided, white blood cells count became to normal limit, patient was discharged from hospital and out- patient department was arranged. As for long term treatment plan for this patient, we considered radioactive iodine therapy or surgical intervention that depend upon patient's choice.

Discussion

Graves' hyperthyroidism results from the production of unique IgG antibodies that bind to and activate the thyroid-stimulating hormone (TSH) receptor on the surface of thyroid follicular cells causing diffuse thyroid enlargement and increased production of thyroid hormones. The measurement of serum TSH-receptor antibodies positive in 90% of patients with presumed Graves' disease, are measured as TSH-receptor binding (TBII) and stimulating antibodies (TSI) which reflect the effect on thyroid function^[1]

Thionamides [Methimazole, Carbimazole, Propylthiouracil] are the most widely used antithyroid drugs. They are given for long periods of time and cause adverse effects in 3 to 5% of patients. In most cases, adverse effects are minor and transient (e.g. skin rash, itching, mild leucopenia)^[2]

The immunological reactions include immunoglobulin E-mediated hypersensitivity reaction, drug-induced immunoglobulin G and M responses and neutrophil-drug complex^[3] Onset is acute and patients present with symptoms and signs of infection together with high fever^[4] After absorption of anti-thyroid drugs, carbimazole is rapidly metabolized to methimazole. ^[5]

Factors indicating bad prognosis in ATDs induced hematopoietic damage are: age >65 years, pancytopenia, coexisting liver and renal insufficiency. Therefore, complete blood counts and liver functions were checked at

specific time i.e at 2 weeks of ATD treatment to guard against ATDs induced agranulocytosis in asymptomatic patient.^[6]

The pathogenic mechanism by which ATDs induce agranulocytosis is not well established but appears immune-mediated.^[7]

Neutropenia can be categorized as mild (absolute neutrophil count [ANC] < 1000–1500/ μL /), moderate (ANC < 500–1000/ μL), or severe (ANC < 500/ μL). Drug-induced agranulocytosis has been defined as ANC < 500/ μL of blood, most patients experience ANC < 100/ μL .^[8]

Thyroidectomy is effective in the management of patients with Graves' disease if failure to medical treatment, since it provides rapid control of hyperthyroidism with a high cure rate.^[9]

Conclusion

Antithyroid drug-induced leucopenia represents a serious complication resulting from the rates of severe infections especially in those cases severe neutropenia^[1] Early ATD-induced neutropenia detection may decrease the severity and mortality when the causative drug is withdrawn.^[10]

Test	Result	Reference range
White blood cells	1380	4400-11,300 cells/ μL
Hemoglobin	13.8	12.2-18.1 g/dL
Red blood cells	4.7	4.04-6.13 M/ μL
Neutrophils	0.9	37-80%
Mean corpuscular volume	84.9	80-97 fL
C-reactive protein	7.6	0-2 mg/L
	Patient's data	Normal value
FT4 (ng/dl)	7.34	0.89-1.76
TSH (ng/dl)	<0.008	0.55-4.78
Ab-TSH receptor (%)	10.90	< 0.12
Thyroglobulin Ab(U/ml)	<15.0	0-60
Anti-TPO Ab (U/ml)	<28.0	0-60

FT4, free thyroxine; TS H, thyroid-stimulating hormone; Anti-TPO Ab, antithyroid peroxidase antibodies;

ANC --Absolute neutrophil count WBC- White blood cell count-

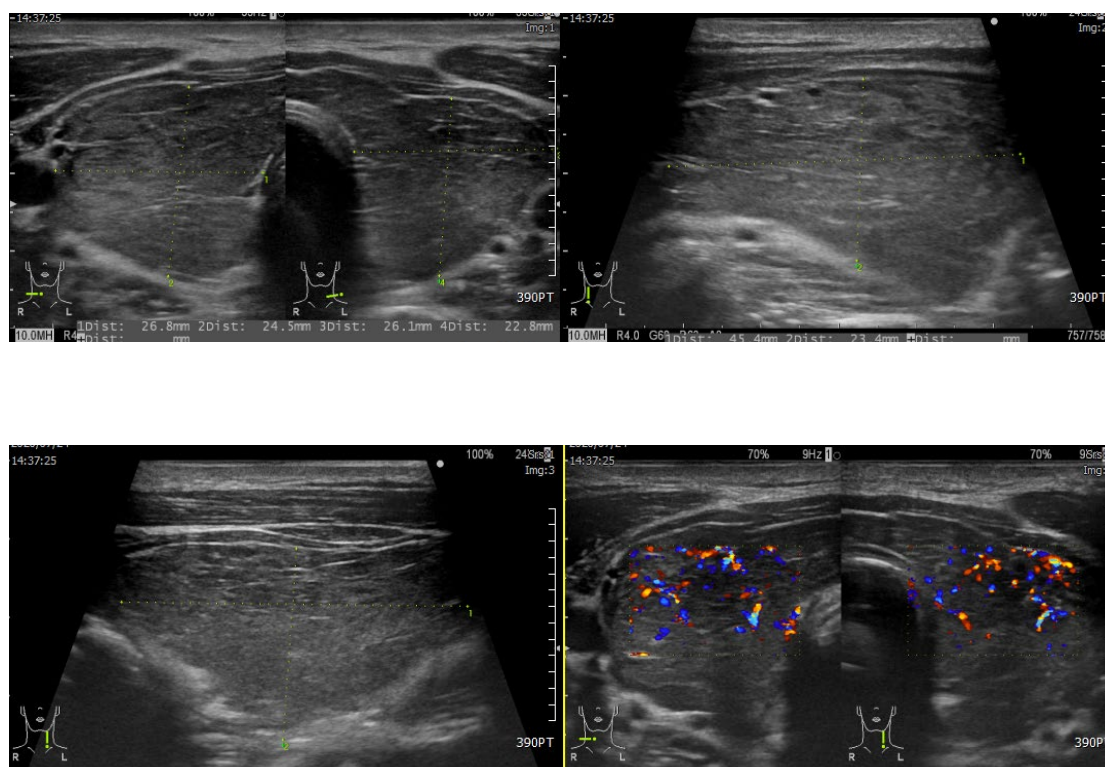
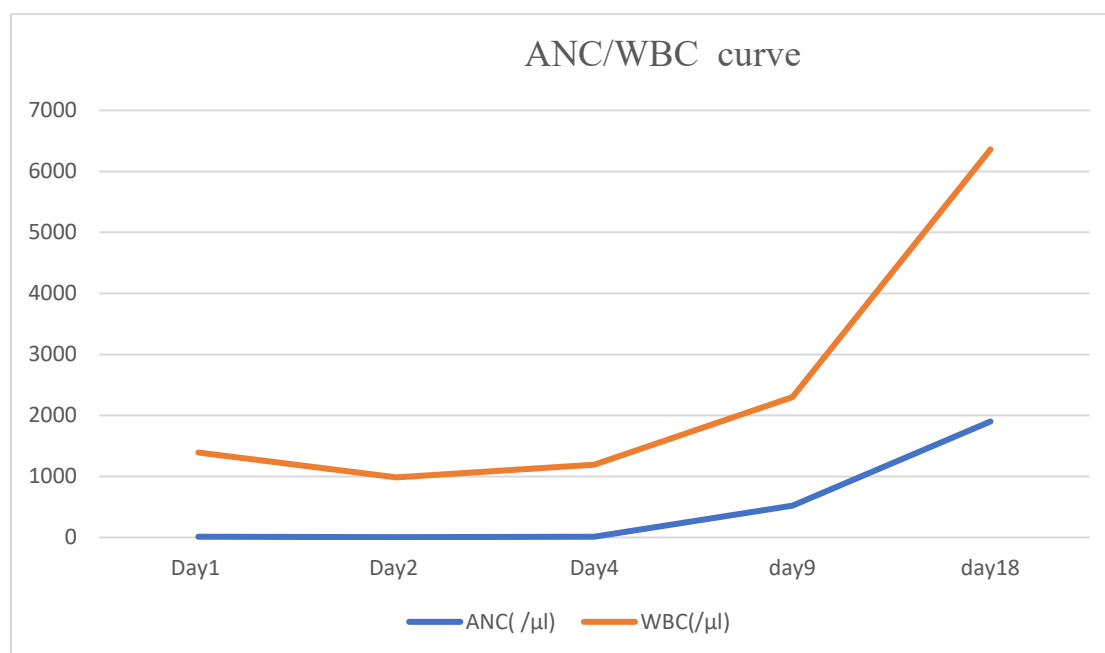


Figure 1. Thyroid sonogram finding-autoimmune picture

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